

FIG. 1

FIG. 2A

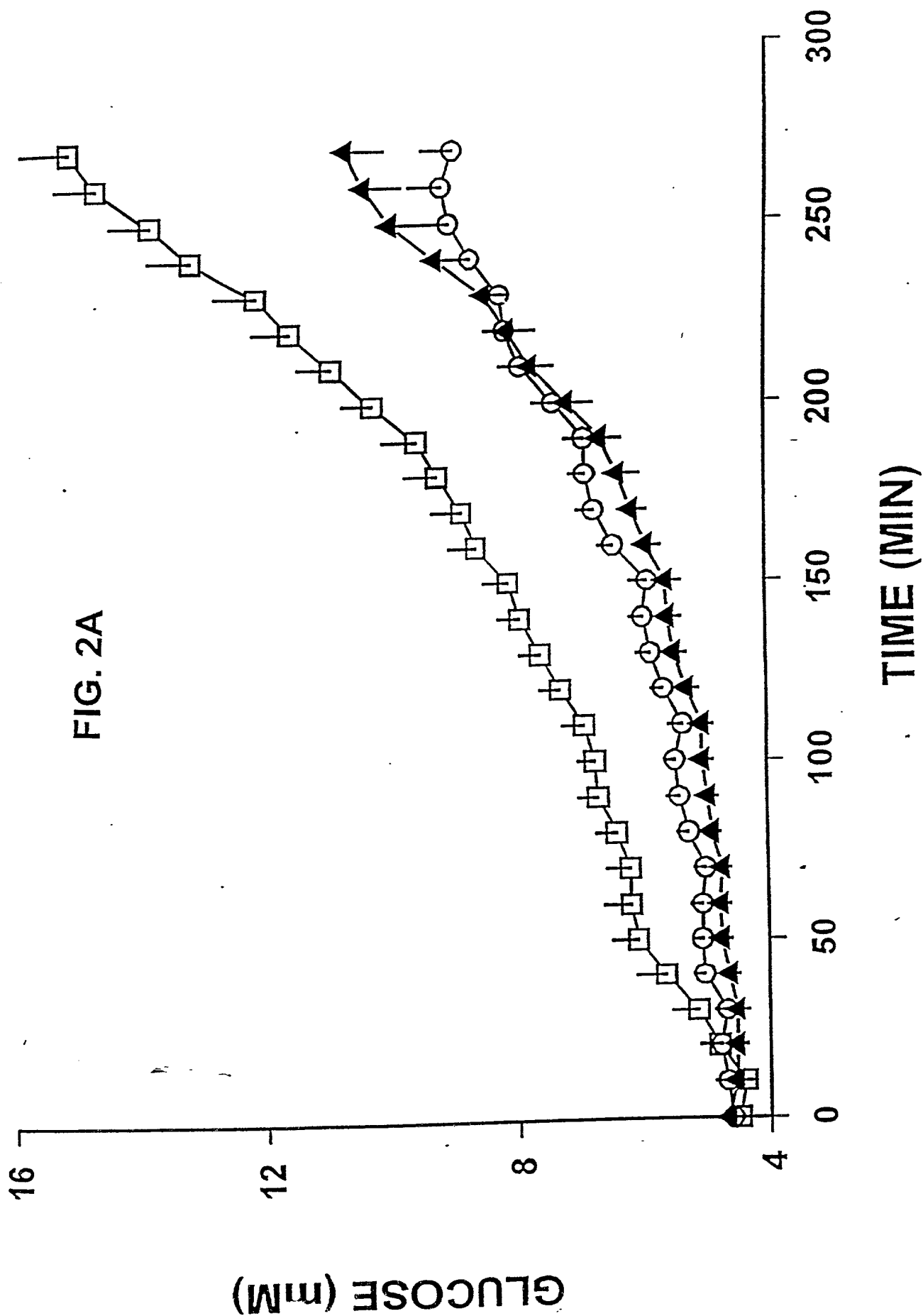


FIG. 2B

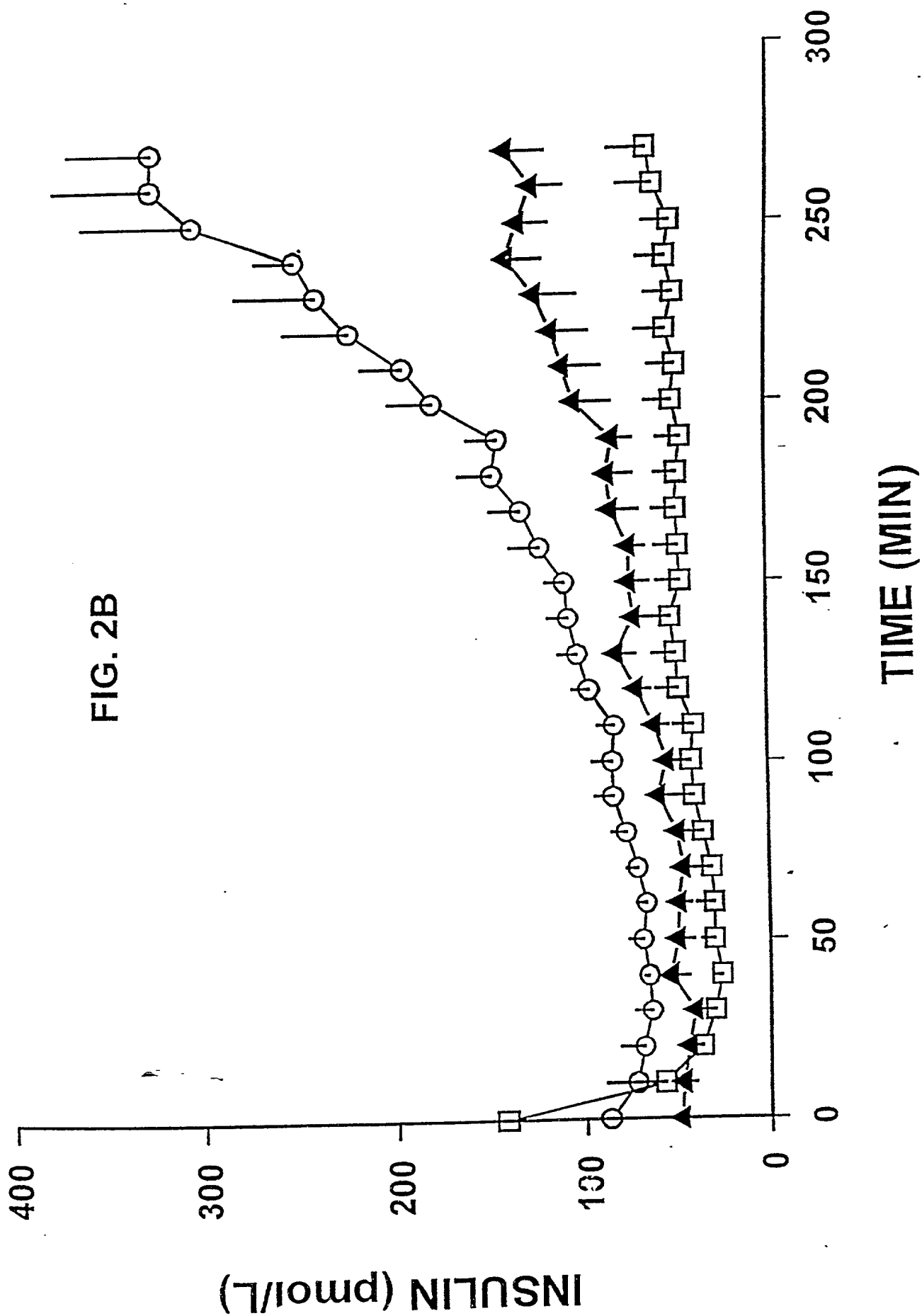
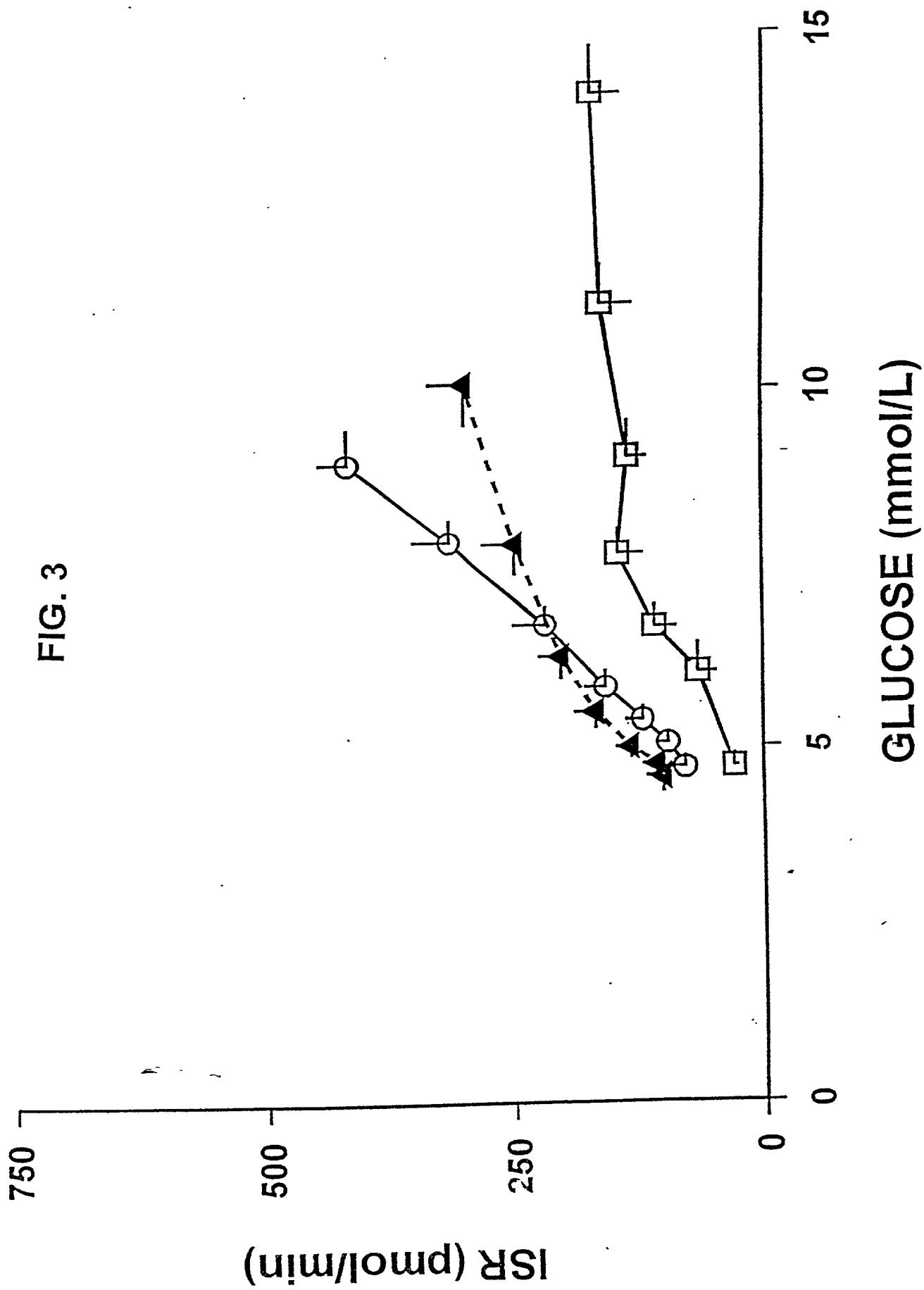
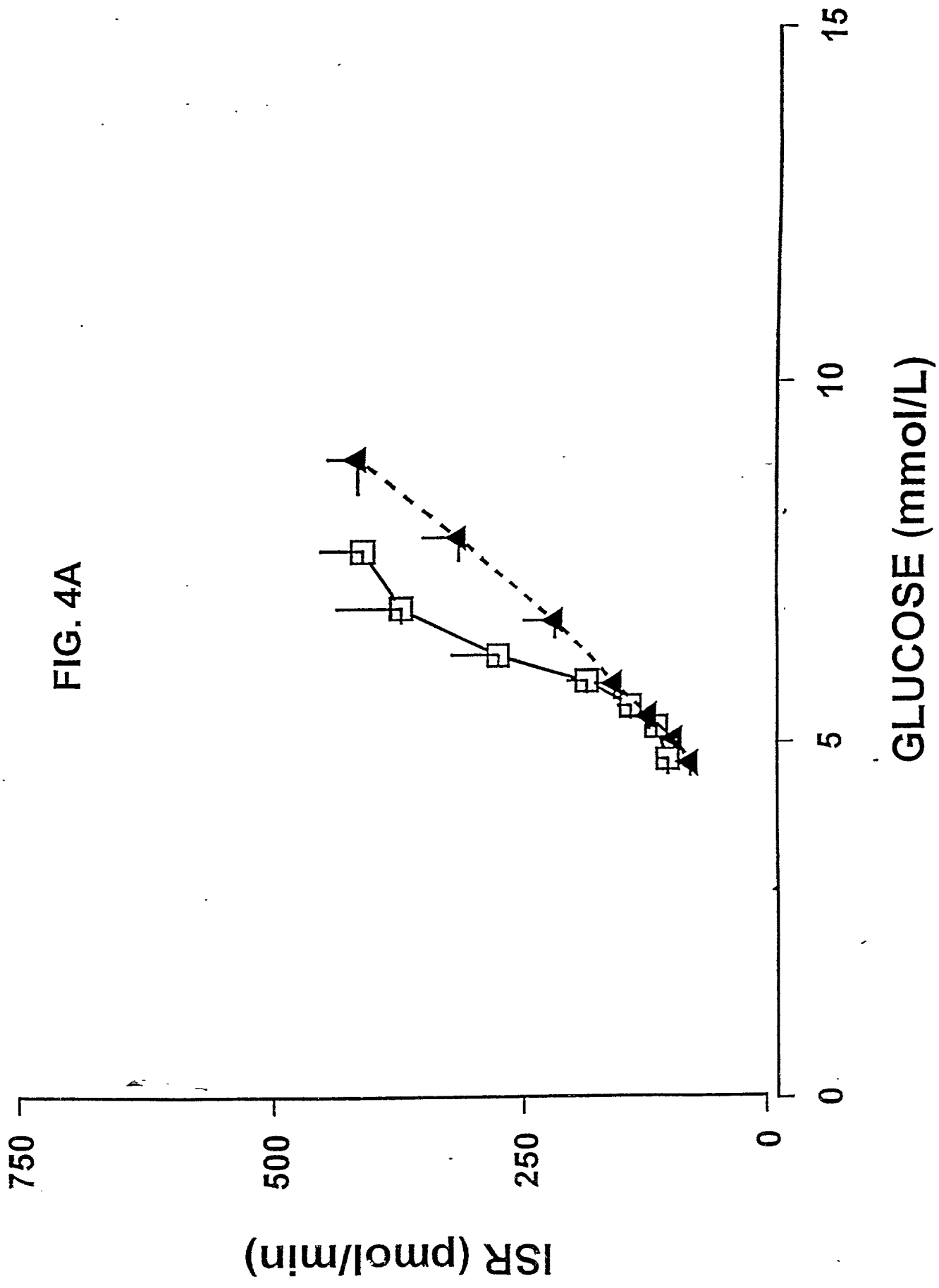
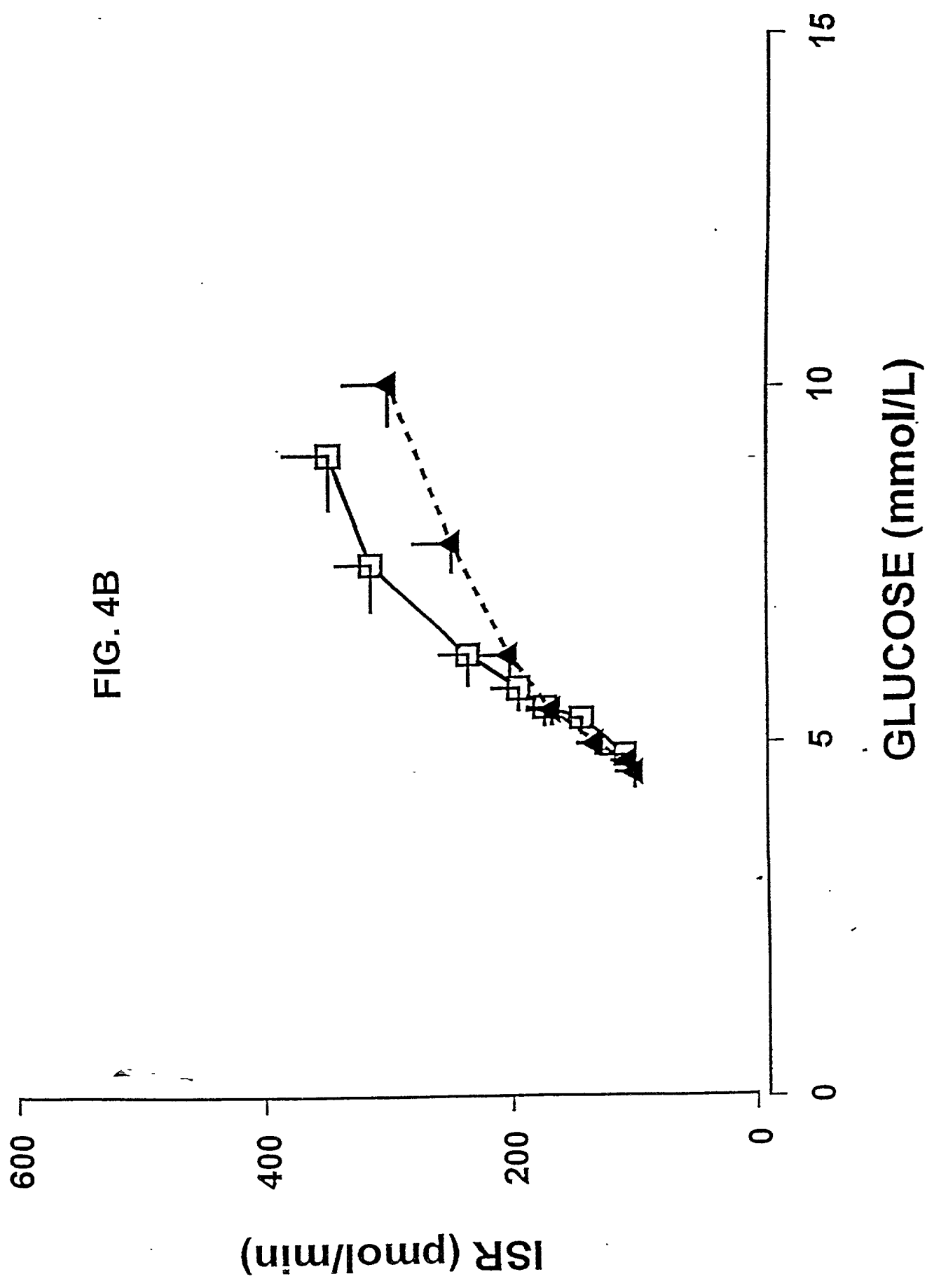
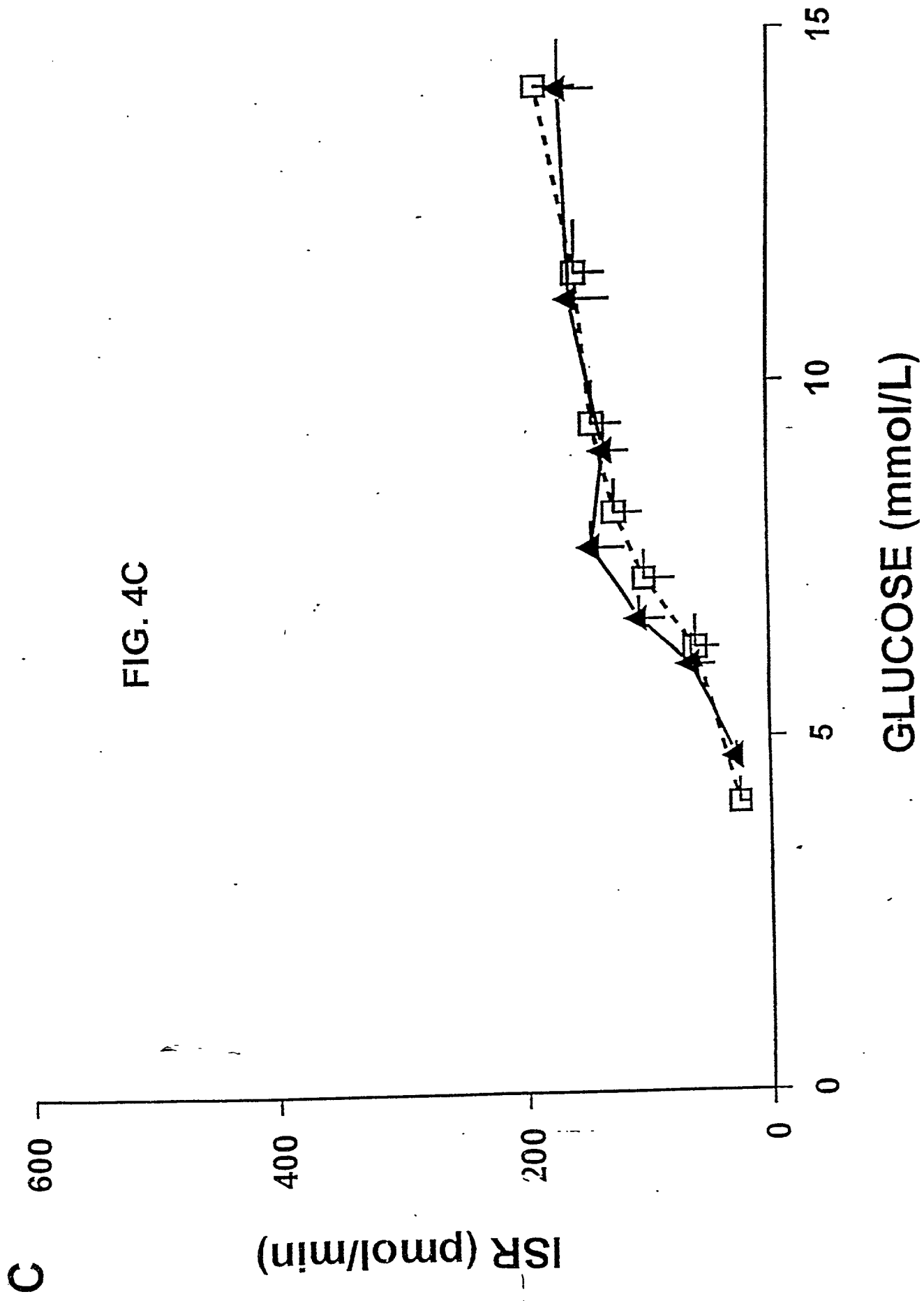


FIG. 3



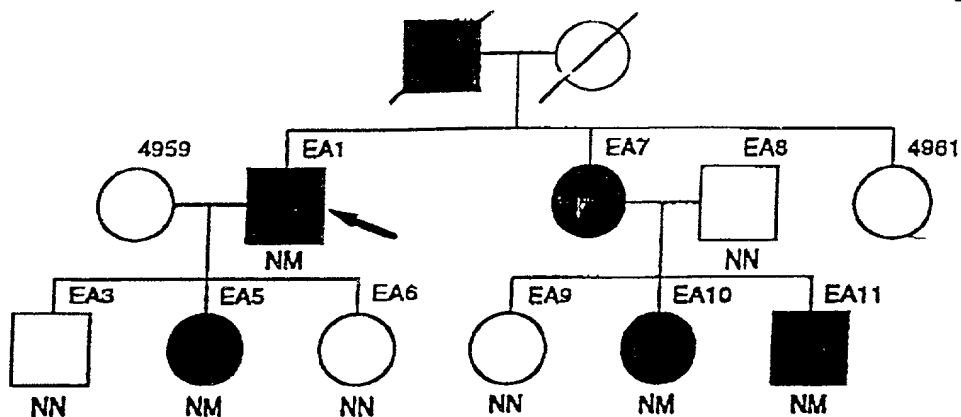






A. Edinburgh Pedigree

FIG. 5A



Frameshift mutation, insertion of C in codon 289, Exon 4; CCC→CCCC

B. H Pedigree

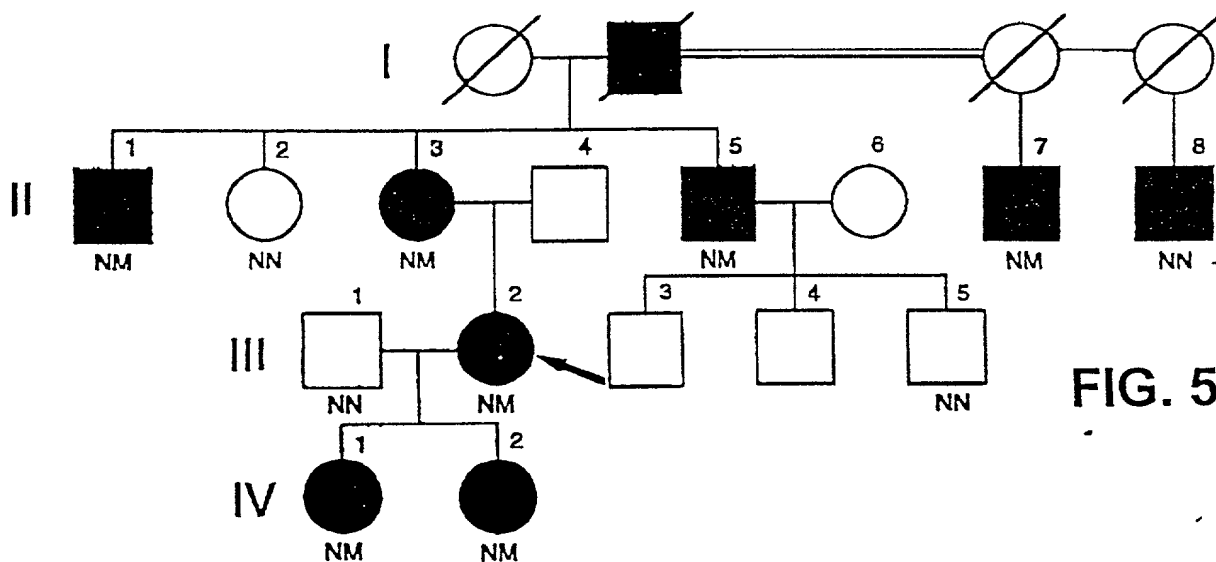
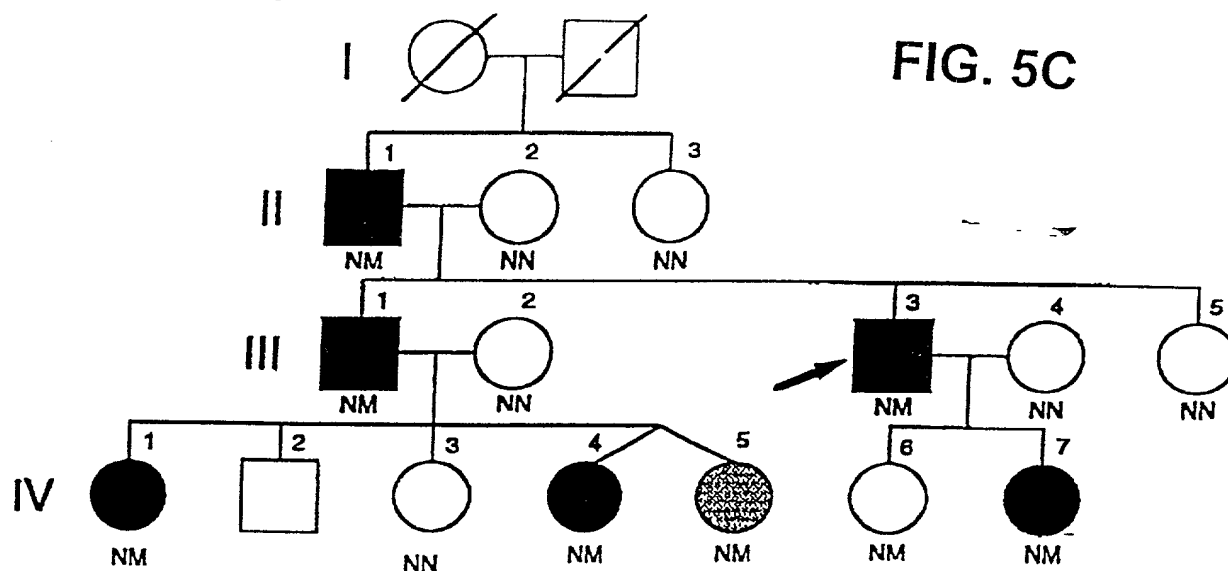


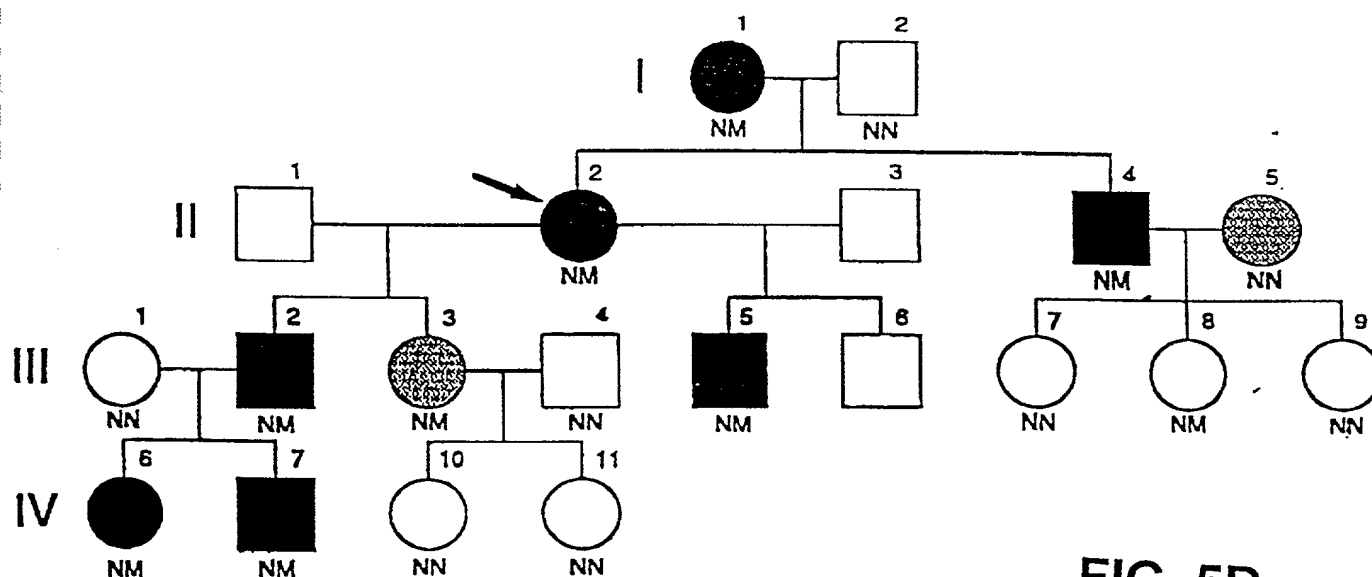
FIG. 5B

Missence mutation, codon 131, Exon 2; CGG (Arg)→CAG (Gln)

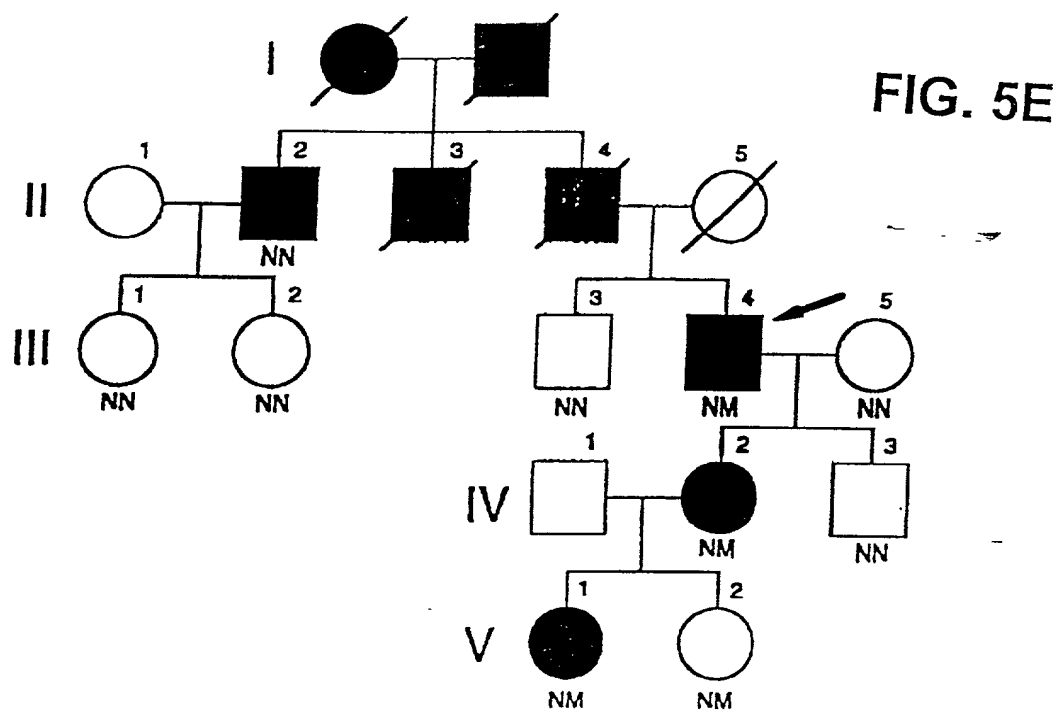
C. P Pedigree



D. GK Pedigree

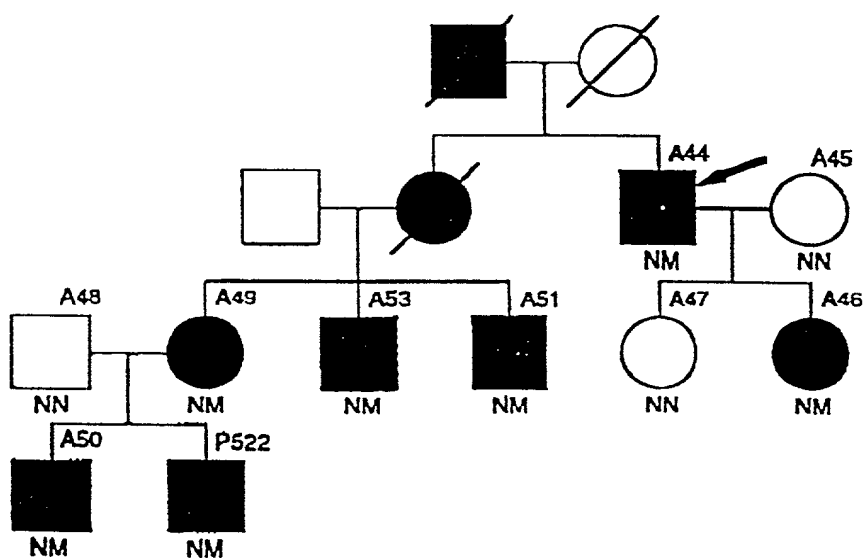


E. Ber Pedigree



Frameshift mutation - deletion of TG in codons 547-548, Exon 9; ACT GAG→ACAG

F. A Pedigree



Missense mutation, codon 447, Exon 7; CCG→CTG, Pro→Leu

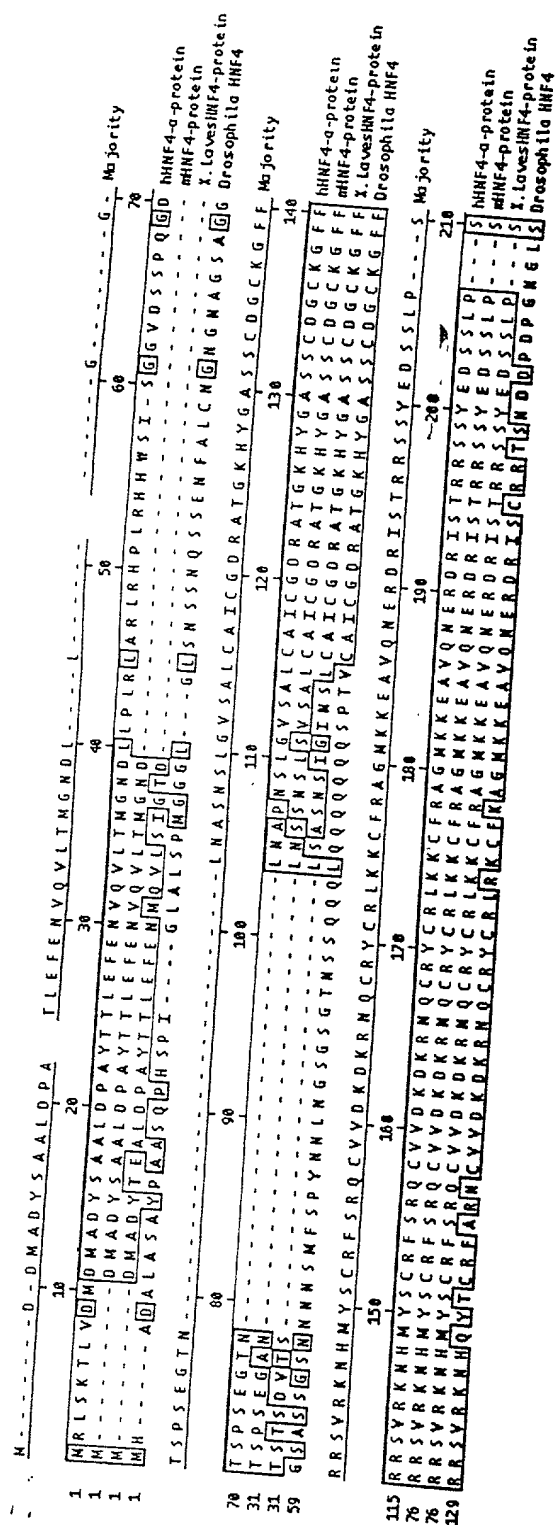
Sample	Time (min)	Temperature (°C)	Pressure (atm)	Flow rate (ml/min)	Detector	Concentration (mg/ml)	Retention time (min)	Peak area (a.u.)	Identification
1	10	100	1	1.0	UV	0.5	12.5	1500	Compound A
2	20	100	1	1.0	UV	0.5	15.0	2000	Compound B
3	30	100	1	1.0	UV	0.5	18.0	1800	Compound C
4	40	100	1	1.0	UV	0.5	20.0	1600	Compound D
5	50	100	1	1.0	UV	0.5	22.0	1400	Compound E
6	60	100	1	1.0	UV	0.5	25.0	1200	Compound F
7	70	100	1	1.0	UV	0.5	28.0	1000	Compound G
8	80	100	1	1.0	UV	0.5	30.0	800	Compound H
9	90	100	1	1.0	UV	0.5	32.0	600	Compound I
10	100	100	1	1.0	UV	0.5	35.0	400	Compound J

—



Frameshift mutation - CT deletion codon 379, Exon 6; CCT→C

FIG. 6



۱۰۰

228	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
229	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
230	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
231	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
232	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
233	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
234	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
235	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
236	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
237	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G	D	I	R	A	K	K	I	A	S	I	D	V	C	E	S	M	K	E	Q	L	L	V	L	V	E	W	A	K	Y	I	P	A	F	C	E	L	P	L	D	D	Q	V	A	M	a	j	o	r	i	t	y
238	I	N	A	L	Q	A	E	V	L	S	Q	I	T	S	P	V	S	-	-	-	G	I	N	G																																																			

Fig. 7B

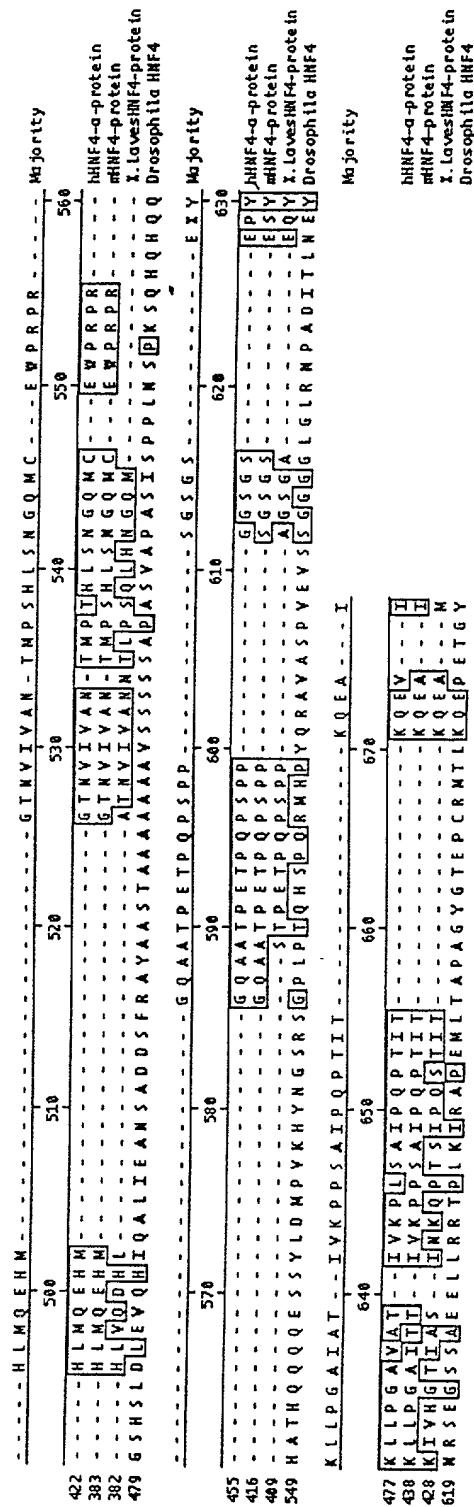


Fig. 7C

FIG. 8A. Partial Sequence of Human HNF4 Gene
(Exon 1 SEQ ID NO:34)

GCAGAGAGGG CACTGGGAGG AGGCAGTGGG AGGGCGGAGG
GCGGGGGCCT TCGGGGTGGG CGCCCAGGGT AGGGCAGGTG
GCCGCGGCGT GGAGGCAGGG AGAATGCGAC TCTCGAAAAC
CCTCGTCGAC ATGGACATGG CCGACTACAG TGCTGCACTG
GACCCAGCCT ACACCACCCT GGAATTTGAG AATGTGCAGG

TGTTGACGAT GGGCAATGGT AGGTGGGGGC AGATGTGCCC
AGGTGTGCCA GTGGGGGCGAG GTGTGCCTGG GTCCAGGAGC
AGATCTTTGG CACTCAACTT TGGGGTGGGA GGAGAATGAT
ACAAAATGGT AGGTTGGTCC TACAGGCCAG CACAGGTGTT
GCCAAGTGAA GCCCATGTGC CCAGGCACAG TGATCACAGG

CATTCTGGGT GAAGGGAGGC CTGCAAGGGC CAATTTCCAG
CAAAAGTCGA TCCCGGCTAT TCCTCCCAGG CCCTTCCAGT
CCTCACTGCC TCACAGTGGC TCTGCTTGGC GCTTGGCACA
GTGACATGAT GGTGAGCTCC CCCTTGGTGC CCAGCTCCAG
CGATTCAGCC CAGCACGGCC CCTTCGTGAA CCCCTTGGGC

CTAGGTTCAG AGAGACGGCA AGGGATGTTG TATCCCTGGA
GATGGTGGTT GGAGACATAA CCGCATTTCT C

FIG. 8B. Partial Sequence of Human HNF4 gene
(Exon 1b SEQ ID NO:36)

TGGATGTTTG TACATGTGTG CTGTGTGTGC GGGTCATAGA
GCACATGTGT TTGTGCATGC GGACCTGTTG GAGTGCCCTG
TTCTTCCTGC ATCTTTATCC TGTATGGGCG TTTTGTCGTG
TGCCCATATT TGTACCTGCT GTGTATATAT GCAGTTCCCT
GTGCTGCGGG CGGGGGTTCAG CGGTCTCTGG TGTGCACGAC

TGCACAGACC CAAATGCAGG ACTCTGTTGT TGCCACTCAC
CAAGTGAGAT TCATATCAGC AACATGTCCG TTTGTCTCTG
AGCAGATTTG TTGCCGCTGC GTCTCGCCAG ATTGAGGCAT
CCCCTCCGAC ATCACTGGAG CATATCTGGA GGGGTGGACA
GTTCTCCACA GGGAGGTAGG GGAAAAGAGG AGGCCCGGAA

ACCCCTCCTG GAGGGAAGAG CCCCATCGGT CCCAGGCCAG
CCTCAGAGGA GAGGGGGCAG GCAGCTGGCT GAGGTCAGCC
TYGCCACCCTG CTTCTTCTG TGTCTTGGAG CCACTCAGCC
AGTATGAGGC TGCAGCTCCA GCTGAGGTCT GGAATCTTGT
GGTCAGCTCA GCTAGGGTGA GGAGGCAGCT GCTGGGCACT

GCTTGTTGTC AGCTCAGCAG GTGCTCACCT GCCCCTGCCG
TCCAGTCACG TGTGACCTTG GGCATGTCAC CTCCCCTATC
CTGGCTTCTG TATCTTCTAC AAAACAGGCT TCATTCCCCC
AGGCCTGCTG GCTGGACGGC TTTTAGGCCT GTCTGAGGAC
CACGCCAGGA GCGCAAGGCA AAAACACACC AGAGAT

FIG. 8C. Partial Sequence of Human HNF4 Gene
(Exon 2 SEQ ID NO:38)

CCCCTTGCGA GTTAGGAGGC CGGCTCCAC CCCAGAAGGT
GGCCAGGTTT TCATGCCTTC CTAGAGAAAG CTGGGGCTGG
TGGCCTCCAC CACAGGGAGA CGCAGACCCT CAGAAACAAG
TCTGTGAAGT CACAACCAGC CCCAGTTTAC AGATGTGAAA
CTGAAGCTCC AAAAAGTCAG GAGGTCACTG AGTGGGGAGG

TGATGGAGTG GAACAGCCCC CAGATCTGGC TGAGGCCGAA
GCCCTGGAGA GATCCCCGCA AGGCTCCCTT AGATGCCTGA
CATTCTGTTC TTCCTGAAGC CTCACTCCCT TCTCTCCTGG -
CGCAGACACG TCCCCATCAG AAGGCACCAA CCTCAACGCG
CCCAACAGCC TGGGTGTCAG CGCCCTGTGT GCCATCTGCG

GGGACCGGGC CACGGGCAAA CACTACGGTG CCTCGAGCTG
TGACGGCTGC AAGGGCTTCT TCCGGAGGAG CGTGCGGAAG
AACCACATGT ACTCCTGCAG GTGAGGAGCC TCAATTTCTT
CAGCTGGGAA ATGGGCACAC TTGGGCTCAT GGCCCCAAGG
TCTGTCTTCT CCCTGAGTGG GTAGGTCCCA GAGACAGCTG

CCCTTCAGGG CCTTCAAGGC TCCTTCTGGTT TTGT

FIG. 8C. Partial Sequence of Human HNF4 Gene

FIG. 8D. Partial Sequence of Human HNF4 Gene
(Exon 3, SEQ ID NO:40)

AGAGAGTTCA TAGCACCTTT CCAGCTCCTG GTGGGTTCAA
GAGAGAACTC CCGGGATGAA GAGATGAGAG CACTGAGGTT
GGGGGGTCAA CTGGATAGCC AGGGCCCTAG TTCTGTCCTA
AGAGGAGGAA GTTGTGTCTT CTCCATCCAA CCATCCAAAAG
ACCTCCCCAG ATTTAGCCGG CAGTGCGTGG TGGACAAAGA

CAAGAGGAAC CAGTGCCGCT ACTGCAGGCT CAAGAAATGC
TTCCGGGGCTG GCATGAAGAA GGAAGGTGAG CCTCGGCCCT
CCCCGCCCCA CCACCACTGC ACCACCTGCA CCCACAGCTC
CCCGACAGTC ATTTACAACT GTAGCCACAC TTTATGACTC
AGTGGCAGGC CCCAGGGTGA CTGGCTAATG GCTGAGAAGA

GGGAGGGCCT GGAAATCTGA CCATAGGGAG CGGCTGGGCT
TGGTCTTGAG AAAGATTC

FIG. 8D-90745260

FIG. 8E. Partial Sequence of Human HNF4 Gene
(Exon 4 SEQ ID NO:42)

tcccactcct catcagtcac agacaccccc accccctact
ccatccctgt tctccctcct cacctctctg tgcctcctca
cagCCGTCCA GAATGAGCGG GACCGGATCA GCACTEGAAG
GTCAAGCTAT GAGGACAGCA GCCTGCCCTC CATCAATGCG
CTCCTGCAGG CGGAGGTCCT GTCCCGACAG GTACCGGGGT

GATCCTGCCA CCCACCCAGG GGATCCCCCA CACTACAGAG
GAGCTCACCT CCTCCACCTC CATTCTCCCC AGCCAGGCCC
TGGAGCAGCT GACGGGAGGG GCCTCAGATA TTACAGAAGG
GACACTGAGT GCGGTTTCAC ATGGCCCAGT TTGCAGCAAG
GGCAGGAATC GAACCTGGCG CCCTGGGGCA CTTTCTAATT

CATCCTACTG CCTGCATCCC ACAGGCCAAG CAGAGTCTTC
ACCTTCACTG AGGGCCTGCG ATCAGCTCAG CTCCGAGAGA
ACAGAGCAGT GGCTCAGTGG AGAGAGGTGG CAAAGTGGGG
CCCAGCCCTT CCCTTGCTGA GTGACCTTGG GCAAGTCACA
GCACCTCTCT GAGCCATGGT TGCCTCATTG TCAGAAAAGG

ATGATGATTT TTTGCCTGC TTCTCCTCTA AGGCTGACAG
ACTCCTTGGG GCTCTAAAGC TG

FIG. 8E-3011526

FIG. 8F. Partial Sequence of Human HNF4 Gene
(Exon 5, SEQ ID NO:44)

TTCTCCTCA TCCCTGCCTC CTCCTCCCT CCGTTTTTAC
CCTGAGCTTC CTTCAGAGCT GGAGGGCACC CACTATCCAG
CCCCCTCCCC ACATCTGATT CCAGGGAGGG GGCTCTGTGC
AGGGGACAGA GAATGCGGGA GGGCCCGGAC ATCTCCAGCA
TTTTCTTCCC TGTATCTCTC GAAGATCACC TCCCCCGTCT

CCGGGATCAA CGGCGACATT CGGGCGAAGA AGATTGCCAG
CATCGCAGAT GTGTGTGAGT CCATGAAGGA GCAGCTGCTG
GTTCTCGTTG AGTGGGCCAA GTACATCCCA GCTTTCTGCG
AGCTCCCCCT GGACGACCAG GTGAGGATGG GCGTGGATGG
TGGGCAGTAG TGGGCAGTGG GCGGGGCAGC CAGGGGGCTG

CTGGCCCACC TGGGATATAG CCGTGGACTG GCTTGATTTT
ATTTTATTTA ACAAATATG TAGTGACAC ACGTGTCTGA
AACTTTAAAT CACCTTACAA ATATTAAGTC AGTTAGCTCC
TCCAACAAC CTATGAGGTA GGTACTAAGG TACTATTATT
ACTGCCATCT CATAGGTGAG AGATTGGGGC ACAGAGAGGT

TAAGTAACCT GCTCAAGGTC ACATAGCTAC TATCCAGCAT
AGCTGGG

FIG. 8F-304260

FIG. 8G. Partial Sequence of Human HNF4 Gene
(Exon 6, SEQ ID NO:46)

ATTTTACAA AGCACCTTC ATAATTCTCC ATAGCTGGTC
CATGGGTGGG AATTTGGGAC CCACAGTTTT GGAACCTTTT
GGGATCATAG ACCTTTTTTGA GAATCTCAAA AAAGAAAAAA
AAGCACACAG AATGTTGCTT ACAGTTTCAT CAGGCACACA
GAAGAGGCC AGCACGAAGC AGTTTCTTGC CCAAGGACAC

AGCAGTTCAA GGACAGAGTC AGCGCGAGGT CTCTCAGCTC
TGAGCACATG TTCTTTCCCC TTCCAGGTTT CTAGTTTTAT
GGGTAGTAGT TTTATGATGC CCATTTTACA GTTCAGGCAG
GTAGAGGCAG AGGGGAGCAT TAAGCTGACT TGCCCAGCGT
CACTGAGTTG GCTACGGGCA GCCTTCCCAA GGGTACAGAT

GGCAAACACT GTTCCTTATC TCTTTCAGGT GGCCCTGCTC
AGAGCCCATG CTGGCGAGCA CCTGCTGCTC GGAGCCACCA
AGAGATCCAT GGTGTTCAAG GACGTGCTGC TCCTAGGTGA
GGCGGCTGCC TGCCCTGGCC AGGGCTCCAG GGAGGGTATG
CCTAGCATGG CACTCACCCA GGCAAGGAGA TTCACATGGT

GGCATGCAAG GGTGAGGGAG ACTAGTCAGG AGTGGCCCTG
TCCTCAGGCT TGCATTGGAG GGCTCCAGGA CTCAGTTTTT
AACTGGGTAC CCCACTCAGA TGCAAGGAAA TGTGGATGCA
AGTCACCAAA TTCCCAGCAT TGAAGTCAGA GCACGATCAG
GGTTATCCCT GGAATTACCT GTGCATCCTT TTTTCTTTTG

ACAGAGTCTT GCTCTGTCAC TCAGGCTGGA GTGCAATGAT
GTGA

FIG. 8H. Partial Sequence of Human HNF4 Gene
(exon 7, SEQ ID NO:48)

GCAACACTAG TATTTTAATA TAACAATGCT ATGAGGGAGC
TCGATTATTT ATCCTCATCT TATAGATAAG AAAACTGAGG
CACAGAGAGG TTAAGTAACT TATCCAATA TAACCAGCTA
TCAGGGGCAG AGCCATTAA GCAGGGCAGT GCAGTTCCAG
AATCTGGTCC TTTAACCTTG ATGCTTTGGT GCCTATCAGG

TGACCTTTGA ATGTCATCGA TCTTGTGAGT CATGTTGGTA
AATGGAGCTT GGGTCATGTG AAAGAGGTCC TAGAAAGCCA
AGTTCCAAGC TCAGCCGGAT GACTCAAGGC AGCTTATCTT
CTGAATCTGG GCCTCAGCTT CCTTACCTGT GAAATGGGAG
TCACCATCCC TGCAGGTCCT CCTCCACAG GCACCAGCTA

TCTTGCCAAC TTAAAAGCCA AACTAGAGG AGAGGGGTCA
ACCAAAGTG ACTTCCCATC CTCCCTCCCT CCCAACCCTT
CCAGGCAATG ACTACATTGT CCCTCGGCAC TGCCCGGAGC
TGGCGGAGAT GAGCCGGGTG TCCATACGCA TCCTTGACGA
GCTGGTGCTG CCCTTCAGG AGCTGCAGAT CGATGACAAT

GAGTATGCCT ACCTCAAAGC CATCATCTTC TTTGACCCAG
GTACAGTGCA CACCTCCTAA GCCATCCCTG ACTCTCTCTC
CAGAACGCTC TGCCAGACTT CTCCTATTGG GTTCTGTACA
CTGAGTTCAC AGCCTCATCT CATGTTAACG ACAGCCAGGA
GAGGCCGTTT TCATTAAACA GATGAGGCAA GTCAAGATT

GAAGAGACAA TATGGCCGGG CGCAGTGGCT CACACCTGTA
ATCCCATCAC TTTGGGAGGC TGAGGCGGGC GGATCACCTG
AGGTCAGGGG TCAAGATGAG CCTGGCTAAC ATGGAGAAAC
CCCATCTCTA CTAAAA

FIG. 8I. Partial Sequence of Human HNF4 Gene
(Exon 8 SEQ ID NO:50)

GTGGCTCTGC CAACAACTGG CTGTGCGACC CAGGACAAGT
CCTATCTTTG CACTGTGTCT GGGTTTCCCC GTGTGTAAGA
TGAGGCGGTT GCTAGGTGCT TATTGGATGC ATTCCTCAAG
TCCCGCCCTC CATCTCCTAT TCCCCTCTCT TCTGGTTTAG
TGCTTTAGGA AATGTGGCAG AAATCTTTTT CTGCCTGTGT

CTAGGAAATC ATAATTCATG CTGGCGTACC CTGGTTGTTG
AGGTCCCTGA ATCCTTGTGC CCACACTGCT GAAGACTCCT
TGTGTGACAC AAGTCAGGGG ACATCTGGGT CTTGACTCCC
CAGATGCTCC AGGTGGACCC TGCTGCCCTC CCTTGCCAC
CCTCTTCCAT TGTAGATGCC AAGGGGCTGA GCGATCCAGG

GAAGATCAAG CGGCTGCGTT CCCAGGTGCA GGTGAGCTTG
GAGGACTACA TCAACGACCG CCAGTATGAC TCGCGTGGCC
GCTTTGGAGA GCTGCTGCTG CTGCTGCCCA CCTTGCAGAG
CATCACGTGG CAGATGATCG AGCAGATCCA GTTCATCAAG
CTCTTCGGCA TGGCCAAGAT TGACAACCTG TTGGAGGAGA

TGCTGCTGGG AGGTCCGTGC CAAGCCCAGG AGGGGCGGGG
TTGGATTGGG GACTCCCCAG GAGACAGGCC TCACACAGTG
AGCTCACCCC TCAGCTCCTT GGCTTCCCCA CTGTGCCGCT
TTGGGCAAGT TGCTTAACCT GTCTGTGCCT CAGTTTCCTC
ACCAGAAAAA TGGGAACAAG GCAATGGTCT ATTTGTTCA

GCACCGAGAA CCTAGCACGT GCCAGTCACT GTTCTAAGTG
CTGGCAATTC AGCAAAGAAC AAGATCTTTG CCCTCGGGGA
GGCTGTGTGT GTGTGATAT GTATGGATGC GTGGATATCT
GTGTATATGC CCGTATGTGC GTGCATGTGT ATATAAAGCC
TCACATTTTA TGATTTTGA

FIG. 8J. Partial Sequence of Human HNF4 Gene
(exon 9, SEQ ID NO:52)

GGGACACATA GATGCTATAA GTAGGTCAGT TGGCTGCAGC
AGAGATGTGG GGGATGAGGC TGAAAGGTGA GGCGGGAGCA
AATGGTTGAA GGACTTGCAC TCCAAGGAGC TTTGAGAGCC
ATTGATTACA TCCATTATGT TACTATGTGA CCAATACATT
ACTCATTAGA ACATTTACGT GATCTCAGAG CTTCCTTATA

TGCACCTTGT TCCTTTCAAC TCACTTTTGT TCTCTTGGTT
TTTTGGGGTC CTCTTAACAC CCTCATGAAG TCTATAGATG
GGAATGGTAC ACCCTAGTTT ACTAACCCAG GAATAGGTAC
CCAACAGGCA CTGCCAATAT TGGATGGGCT GGTTGATTGG
CCACGCCTGA GGAAGATGGC GTCCCAAGGC CTGAGGTCTG

CATCCCAGAC TCTCCATCCT GATCGACCTT CTCTACCTGC
AGGGTCCCCC AGCGATGCAC CCCATGCCCA CCACCCCCTG
CACCTCACC TGATGCAGGA ACATATGGGA ACCAACGTCA
TCGTTGCCAA CACAATGCCC ACTCACCTCA GCAACGGACA
GATGTGTGAG TGGCCCCGAC CCAGGGGACA GGCAGGTGGG

CAAACCTCTGG GATTTTACCT TGCAAAGGGT GAGGATGGGG
CTTAAGACAG GAGGCAGGAG AAAGTGGAGT CTAGAAGGTA
GAACCAGGAT GCAACAGTTT TCTGGGTTCC AGGGTAGGGA
ATAAAGGGCA AGATTGTCCA TTTGTTGAGG CTGTTTATTC
AGTAAGGTGA CTGACAGCCT TTAAGTAATG AAGCCATTGT

TGGGATGAGG CAATCCACTG GATGAGGTAA CCCATTGGGT
GAAGATGTCT TGGGTGAGAA TTCCATTAGT TGACATTGTC
CATTAAAGTAA AAGTGGTCAT TGAAGTAAGG CTGCACAGTT
GGGTAAGGCT ATCCATTAGA CATTAGATGA GACTACCCAT
TGGGTCAGGA TGTCTGCTGG GCTA

FIG. 8K. Partial Sequence of Human HNF4 Gene
(Exon 10 SEQ ID NO:54)

TTTGGGAGAA GCAGTCCAAG TCTGCATATC AAATAAATGA
TGGAGGAGAT GGGTGGTAGG ACCTTCCAGA CCTCATAAAA
CTTAGGCTTT ATGATCTGGG ACTCACAGAA GGTGAGCAA
TAAAAGACCT TAGGGATTAT CTGGCTTAAT TAATTCTCTC
ATTTTATAGA GGAAGAAATT AAGTCAAGGT GGGGCAGGGT

GGGAGGGGAG AACTTTCCCG GGGCTCTTCA TTTACTCCCA
CAAAGGCTGG AATTTTGAGC AGCCCCTGTC TGTCTGTTTG
TCCTTCCAGC CACCCCTGAG ACCCCACAGC CCTCACCGCG
AGGTGGCTCA GGGTCTGAGC CCTATAAGCT CCTGCCGGGA
GCCGTCGCCA CAATCGTCAA GCCCCTCTCT GCCATCCCCC

AGCCGACCAT CACCAAGCAG GAAGTTATCT AGCAAGCCGC
TGGGGCTTGG GGGCTCCACT GGCTCCCCC AGCCCCCTAA
GAGAGCACCT GGTGATCACG TGGTCACGGC AAAGGAAGAC
GTGATGCCAG GACCAGTCCC AGAGCAGGAA TGGGAAGGAT
GAAGGGCCCC AGAACATGGC CTAAGGCACA TCCCACTGCA

CCCTGACGCC CTGCTCTGAT AACAAGACTT TGACTTGGGG
AGACCCTCTA CTGCCTTGGA CAACTTTCTC ATGTTGAAGC
CACTGCCTTC ACCTTCACCT TCATCCATGT CCAACCCCCG
ACTTCATCCC AAAGGACAGC CGCCTGGAGA TGACTTGAGC
CTTACTTAAA CCCAGCTCCC TTCTTCCCTA GCCTGGTGCT

TCTCCTCTCC TAGCCCCGGT CATGGTGTCC AGACAGAGCC
CTGTGAGGCT GGGTCCAATT GTGGCACTTG GGGCACCTTG
CTCCTCCTTC TGCTGCTGCC CCCACCTCTG CTGCCTCCCT
CTGCTGTCAC CTTGCTCAGC CATCCCGTCT TCTCCAACAC
CACCTCTACA GAGGCCAAGG AGGCCTTGGA AACGATTCCC

CCAGTCATTC TGGGAACATG TTGTAAGCAC TGACTGGGAC
CAGGCACCAG GCAGGGTCTA GAAGGCTGTG GTGAGGGAAG
ACGCCTTTCT CCTCCAACCC AAC

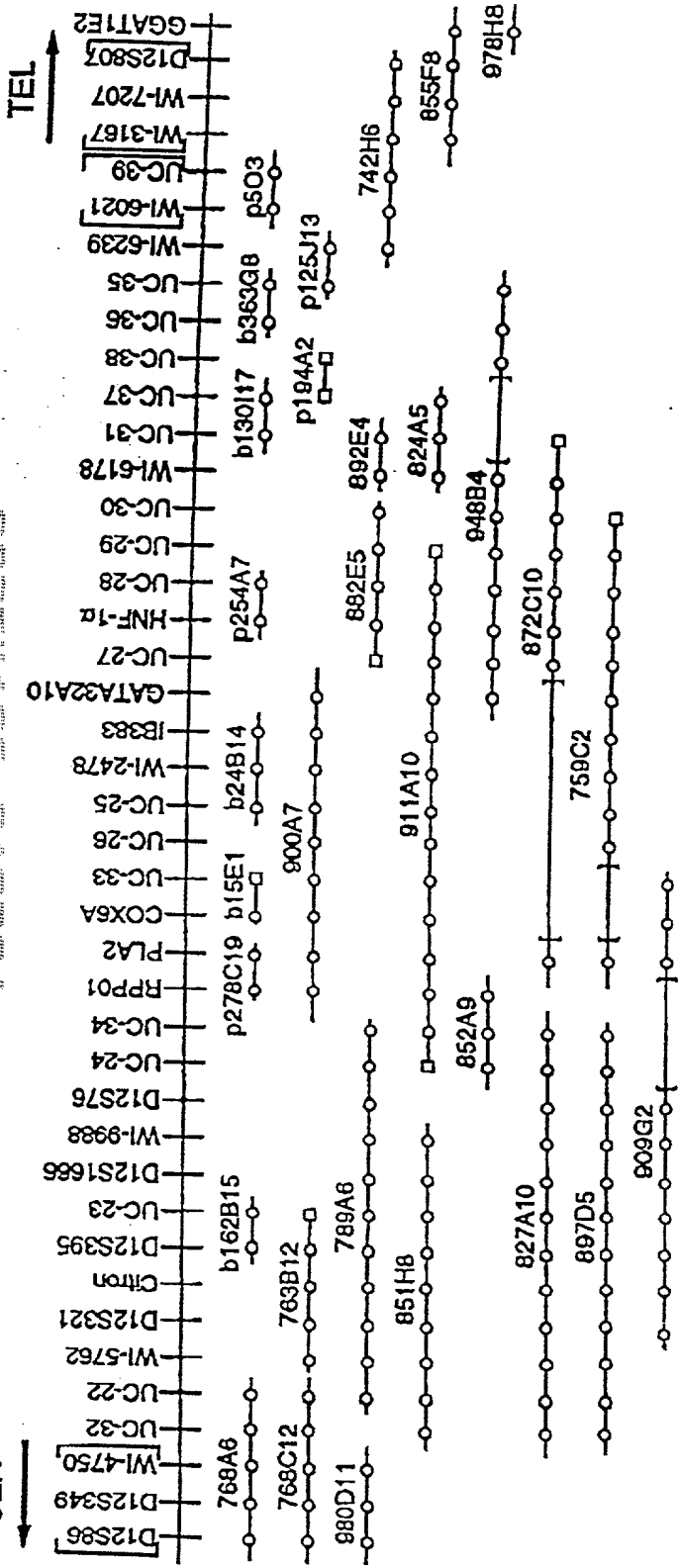


Fig. 9

Fig. 10A

Normal Allele

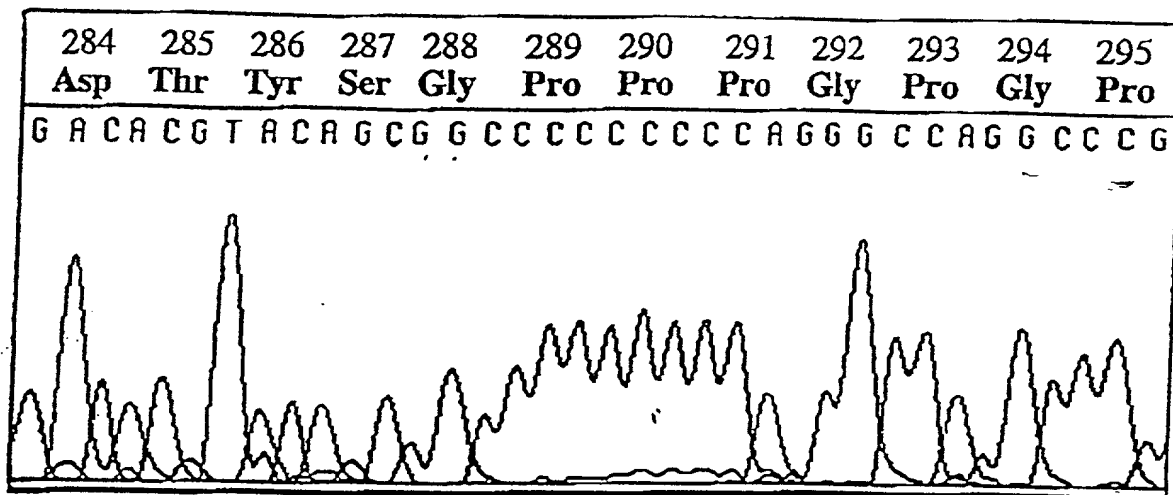


Fig. 10B

. Mutant Allele

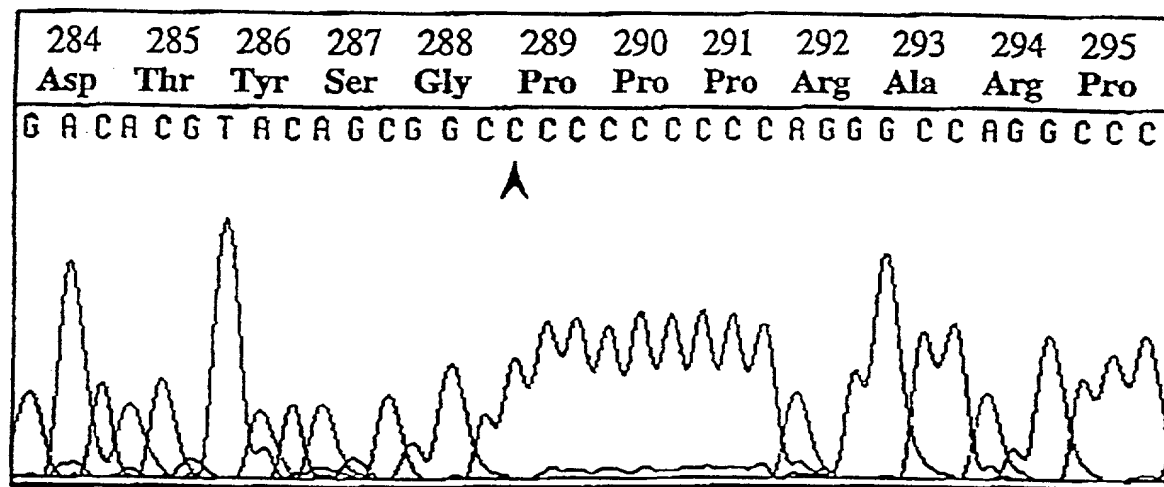


FIG. 11. Translation of human HNF1a sequence (cDNA=SEQ ID NO:1 and protein=SEQ ID NO:2)

1	Met Val Ser Lys Leu Ser Gln Leu Gln Thr Glu Leu Leu Ala Ala Leu Leu Glu Ser Gly Leu Ser Lys Glu	10
20	ATG GTT TCT AAA CTG ACC CAG CTG CAG ACC GAG CTC CTG GCG GCC CTG CAG TCA GGG CTG ACC AAA GAG	
30		40
50	Ala Leu Ile Gln Ala Leu Gly Glu Pro Tyr Leu Leu Ala Gly Glu Gly Pro Leu Asp Lys Gly Glu Ser Cys Gly Gly Arg	
	GCA CTG ATC CAG GCA CTG GGT GAG CCG GGG CCC TAC CTC CTG GCT GGA GAA GGC CCC CTG GAC AAG GGG GAG TTC TEC GGC GGC CCA	
60		70
80	Gly Glu Leu Ala Glu Leu Pro Asn Gly Leu Gly Glu Thr Arg Gly Ser Glu Asp Glu Thr Asp Asp Gly Glu Asp Phe Thr Pro Pro	
	GAG CTG GCT GAG CTG CCC AAT GGG CTG GGG GAG ACT CCG GGC TTC GAG GAC CAG ACC GAC GAC GAT GGG GAA GAC TTC ACC CCA CCC	
90		100
Exon 1/ 110 Exon 2		
	Ile Leu Lys Glu Leu Glu Asn Leu Ser Pro Glu Glu Ala Ala His Gln Lys Ala Val Val Glu Thr Leu Leu Gln Glu Asp Pro Trp Arg	
	ATC CTC AAA GAG CTG GAG AAC CTC ACC CCT GAG GAG GCG GCC CAC CAG AAA GCC GTG GTG GAG ACC CTT CTG CAG GAG GAC CCG TGG CGT	
120		140
	130 Gln (Hinek- missense)	

Val Ala Lys Met Val Lys Ser Tyr Leu Gln Gln His Asn Ile Pro Gln Arg Glu Val Val Asp Thr Thr Gly Leu Asn Gln Ser His Leu
GTG GCG AAG ATG GTC AAG TCC TAC CTG CAG CAG CAC AAC ATC CCA CAG CCG GAG GTG GTC GAT ACC ACT GGC CTC AAC CAG TCC CAC CTG

A

150

160

170

Exon 2

Ser Gln His Leu Asn Lys Gly Thr Pro Met Lys Thr Gln Lys Arg Ala Ala Leu Tyr Thr Trp Tyr Val Arg Lys Gln Arg Glu Val Ala
TCC CAA CAC CTC AAC AAG GGC ACT CCC ATG AAG ACG CAG AAG CCG GGC CTC TAC ACC TGG TAC GTC CCG AAG CAG CGA GAG GTG GCG

Exon 3

180

190

200

Gln Gln Phe Thr His Ala Gly Gln Gly Gly Leu Ile Glu Glu Pro Thr Gly Asp Glu Leu Pro Thr Lys Lys Gly Arg Arg Asn Arg Phe
CAG CAG TTC ACC CAT GCA GCG CAG GGA GCG CTG ATT GAA GAG CCC ACA GGT GAT GAG CTA CCA ACC AAG AAG GCG CCG AAG AAC CGT TTC

210

220

230

Lys Trp Gly Pro Ala Ser Gln Gln Ile Leu Phe Gln Ala Tyr Glu Arg Gln Lys Asn Pro Ser Lys Glu Glu Arg Glu Thr Leu Val Glu
AAG TGG GGC CCA GCA TCC CAG CAG ATC CTG TTC CAG GGC TAT GAG AAG CAG AAG AAC CCT ACG AAG GAG CAG CGA GAG ACG CTA GTG GAG

Exon 3 | 240 Exon 4

250

260

Glu Qys Asn Arg Ala Glu Qys Ile Gln Arg Gly Val Ser Pro Ser Gln Ala Gln Gly Leu Gly Ser Asn Leu Val Thr Glu Val Arg Val
CAG TCC AAT AGG GCG GAA TGC ATC CAG AGA GCG GTG TCC CCA TCA CAG GCA CAG GCG CTG GGC TCC AAC CTC GTC ACG GAG GTG CGT GTC

270

280

290

Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu Glu Ala Phe Arg His Lys Leu Ala Met Asp Thr Tyr Ser Gly Pro Pro Gly Pro Gly

TAC AAC TGG TTT GCC AAC CCG CCG AAA GAA GAA GCC TTC CCG CAC AAG CTG GCC ATG GAC AGG TAC AGC GGG CCC CCC CCA GGG CCA GGC

CCCC (Donoghue - C insertion)

Pro Gly Pro Ala Leu Pro Ala His Ser Ser Pro Gly Leu Pro Pro Pro Ala Leu Ser Pro Ser Lys Val His Gly Val Arg Gly Gln
CCG GGA CCT GCG CTG CCC GCT CAC AGC TTC CCT GGC CTG CCT CCA CCT GGC CTC TCC CCC AGT AAG GTC CAC G|GT GTG CCG TNT GGA CAG

Exon 4 | 320 Exon 5

330

340

Pro Ala Thr Ser Glu Thr Ala Glu Val Pro Ser Ser Ser Gly Gly Pro Leu Val Thr Val Ser Thr Pro Leu His Gln Val Ser Pro Thr
CCT GCG ACC AGT GAG ACT GCA GAA GTA CCC TCA AGC AGC GGC GGT CCC TTA GTG ACA GTG TCT ACA CCC CTC CAC CAA GTG TCC CCC ACG

(Pratt - mutation splice acceptor site Exon 6, AG --> GG)

360

Exon 5 | 370 Exon 6

Gly Leu Glu Pro Ser His Ser Leu Leu Ser Thr Glu Ala Lys Leu Val Ser Ala Ala Gly Gly Pro Leu Pro Pro Val Ser Thr Leu Thr
GGC CTG GAG CCC AGC CAC AGC CTG CTG AGT ACA GAA GCC AAG CTG| GTC TCA GCA GCT GGG GGC CCC CTC CCC CCT GTC AGC ACC CTG ACA

C-- (Newton - CT deletion)

Ala Leu His Ser Leu Glu Gln Thr Ser Pro Gly Leu Asn Gln Gln Pro Gln Asn Leu Ile Met Ala Ser Leu Pro Gly Val Met Thr Ile
GCA CTG CAC AGC TTG GAG CAG ACA TCC CCA GGC CTG AAC CAG CAG CCC CAG AAC CTC ATC ATG GGC TCA CTT CCT GGG GTC ATG ACC ATC

420

430

Exon 6 | Exon 7 440

Gly Pro Gly Glu Pro Ala Ser Leu Gly Pro Thr Phe Thr Asn Thr Gly Ala Ser Thr Leu Val Ile Gly Leu Ala Ser Thr Gln Ala Gln
GGG CCT GGT GAG CCT GCC TTC CTG GGT CCT ACG TTC ACC AAC ACA GGT GCC TTC ACC CTG GTC ATC G|GC CTG GCC TTC ACG CAG GCA CAG

450

460

470

Ser Val Pro Val Ile Asn Ser Met Gly Ser Ser Leu Thr Thr Leu Gln Pro Val Gln Phe Ser Gln Pro Leu His Pro Ser Tyr Gln Gln
AGT GTG CCG GTC ATC AAC AGC ATG GGC AGC AGC CTG ACC ACC CTG CAG CCC GTC CAG TTC TCC CAG CCG CTG CAC CCC TTC TAC CAG CAG

480

490

Exon 7 500 | Exon 8

Pro Leu Met Pro Pro Val Gln Ser His Val Thr Gln Ser Pro Phe Met Ala Thr Met Ala Gln Leu Gln Ser Pro His Ala Leu Tyr Ser
CCG CTC ATG CCA CCT GTG CAG AGC CAT GTG ACC CAG AGC CCC TTC ATG GCC ACC ATG GCT CAG CTG CAG AGC CCC CAC G|CC CTC TAC AGC

510

520

530

His Lys Pro Glu Val Ala Gln Tyr Thr His Thr Gly Leu Leu Pro Gln Thr Met Leu Ile Thr Asp Thr Thr Asn Leu Ser Ala Leu Ala
CAC AAG CCC GAG GTG GCC CAG TAC ACC CAC AAG GGC CTG CTC CCG CAG ACT ATG CTC ATC ACC GAC ACC ACC AAC CTG AGC GCC CTG GCC

Exon 8 540 | Exon 9

550

560

Ser Leu Thr Pro Thr Lys Gln| Val Phe Thr Ser Asp Thr Glu Ala Ser Ser Glu Ser Gly Leu His Thr Pro Ala Ser Gln Ala Thr Thr
AGC CTC ACG CCC ACC AAG CAG| GTC TTC ACC TCA GAC ACT GAG GCC TTC AGT GAG TTC GGG CTT CAC ACG CCG GCA TCT CAG GCC ACC ACC

570

580

Exon 9 | 590 Exon 10

Leu His Val Pro Ser Gln Asp Pro Ala Gly Ile Gln His Leu Gln Pro Ala His Arg Leu Ser Ala Ser Pro Thr| Val Ser Ser Ser Ser

CTC CAC GTC CCC AGC CAG GAC CCG GGC ATC CAG CAG CTG CAG CCG GGC CAC CCG CTC AGC GGC AGC CCC ACA| GTG TCC TCC AGC AGC

600

610

620

Leu Val Leu Tyr Gln Ser Ser Asp Ser Ser Asn Gly Gln Ser His Leu Leu Pro Ser Asn His Ser Val Ile Glu Thr Phe Ile Ser Thr
CTG GTG CTG TAC CAG AGC TCA GAC TCC AGC AAT GGC CAG AGC CAC CTG CCA TCC AAC CAC AGC GTC ATC GAG ACC TTC ATC TCC ACC

630 631

CAG ATG GGC TCT TCC CAG TAACACGCGACCTTGGGCCCTGGGCCCTGTACTGGCCTGCTTGGGGGGTGTATGAGGGACAGAGCCAGCCCTGCTGGAGGAACCTGAGCCTGGCG

AGCAACGGTGGCCCTTCCCTGGACAGCTGTGGCCTGGCTGCCACCTCTGCTGATGATCAGAAAGGAGAGGGCTCTGAGGGGCCCAACCCGTGGAGGGCTGCTGGGGGTGCACAGGAGGGG

GTCTGGAGAGCTAGGAGCAAGGCCGTGTATGGCAGATGTAGAGAGGACTGTGGCTGGCTTGGTGGATACAGTCTTCTTACTTGGAACTGAGGGGGGGGGCTATGACTTGGGCAACCC

CAGCCTGGGCCCTATGGAGAGCCCTGGGACCGCTACACCACTCTGGGAGCCACACTTCTAGGACAGAGGCCCTGTGTAGCTGTGTGACCTGTGTGAGCTCTGAGAGGCCCTGGATCAGCGTGGC

CTTGTCTGTCAACCAATGTACCAACGGGGCCACTCCCTTCCCTGGCCCACTCCCTTCCAGCTAGTGAACCAATGGCCATTGTACTGACCCCAATCACCCTACTCACAAGGCAATTTCCTGGGT

GGCTACTCTGTGGCAAGGCCCTGGGGCTCTACTGTCCCTGAGCCCAAGGAGGCCGAGCTAACAGGGAAGGCAAGGCAAGGGCTCTCCTGGTCTTCCCATGCCCAAGCGATTCCCTCTCCCAAGGC

CCCATGACCTCCAGCTTTCCTGTATTTCTTCCCAAGACAATGATGCCCTCTGAGCCCAAGCCCTGGCCCTCCCTGGCTCTACTGGGAAGGCTACTTGGGGGCTGGGAAGTGTCCCTTACTCCTGT

GGGAGCCTGGCAACCCGTGGCAAGTCCAGGTTCCCTGGTGGGGGAGCTCCCTGTCTGTCTGAGGGCCCTGGAGAACCCCTGGCTTGTTTGGGGCAAGAGTACGTGAGCTCACAAGGCCAGCAAGGC

CCGAGCAGCTGAGCAGGGCCGGGGAATGGGCCAGCTTGGTGGTCCCAAGGAGAGAAAGAGGTGACCCCAAGGGTGAACCCCAAGGGCAAGGAGCTTAACTCAGAAAGCCTGGGTG

Sequence alignment

CCTGECTGECTGAGGGAGTTTGGCAGCCACCCCTGAGGAGTCTGAGGTCCCTGACCACTGCCCAGGACGGACAAAGGAGCCTGTGAAACCCAGGACAGCCATGGTCCACATCCCTGGGCCCTGEC

TGCTGAGAACCTGGCCCTTCAGTGTACCGGCTCTACCCCTGGGATTTCAGGAAAGGCCCTGGGGTGAACCGGCAACCCCTGCACTTGTAAGCAAGCCGGGGGAGTGGCAGTTTATTAACT

TTTAGTAAAGTCAAGGAGAAATGGGGTGG

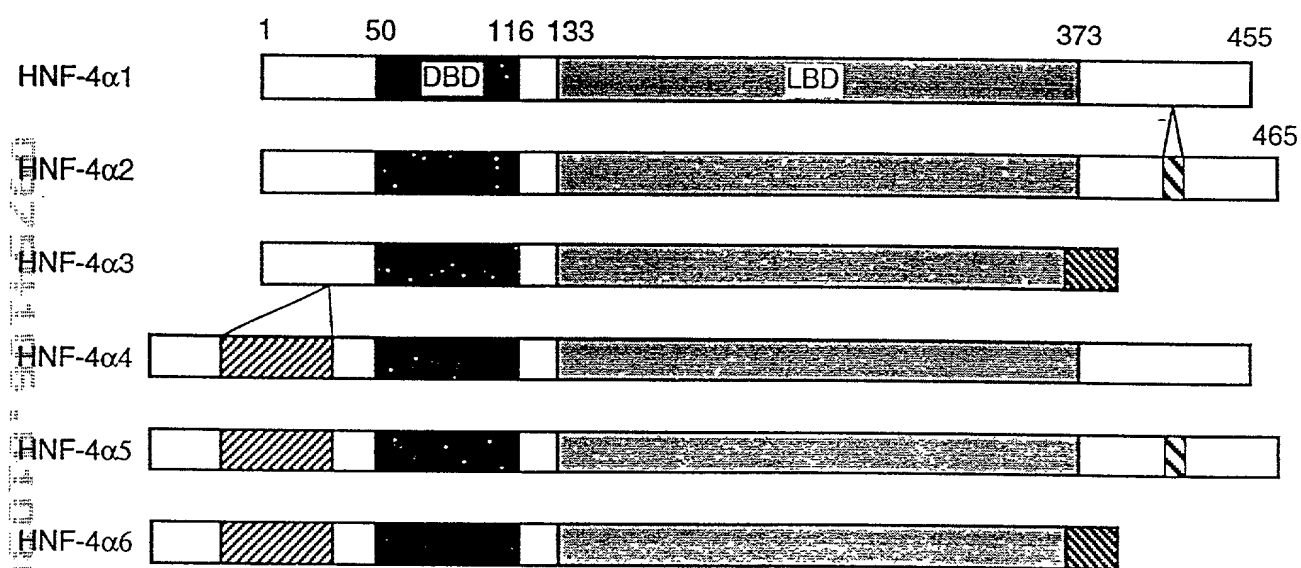
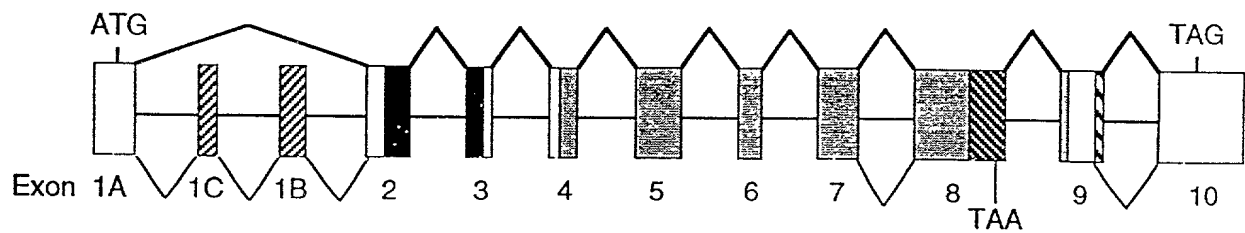


Fig. 12

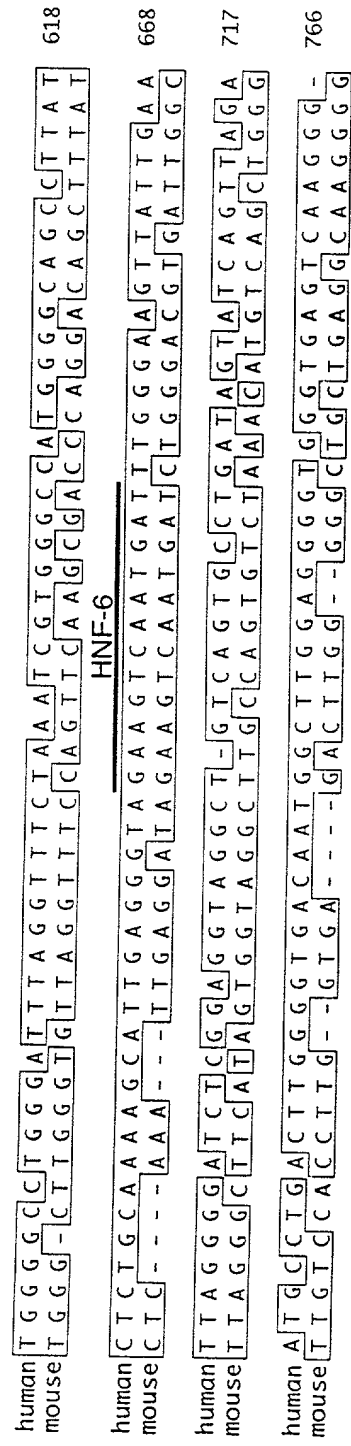


Fig. 13A

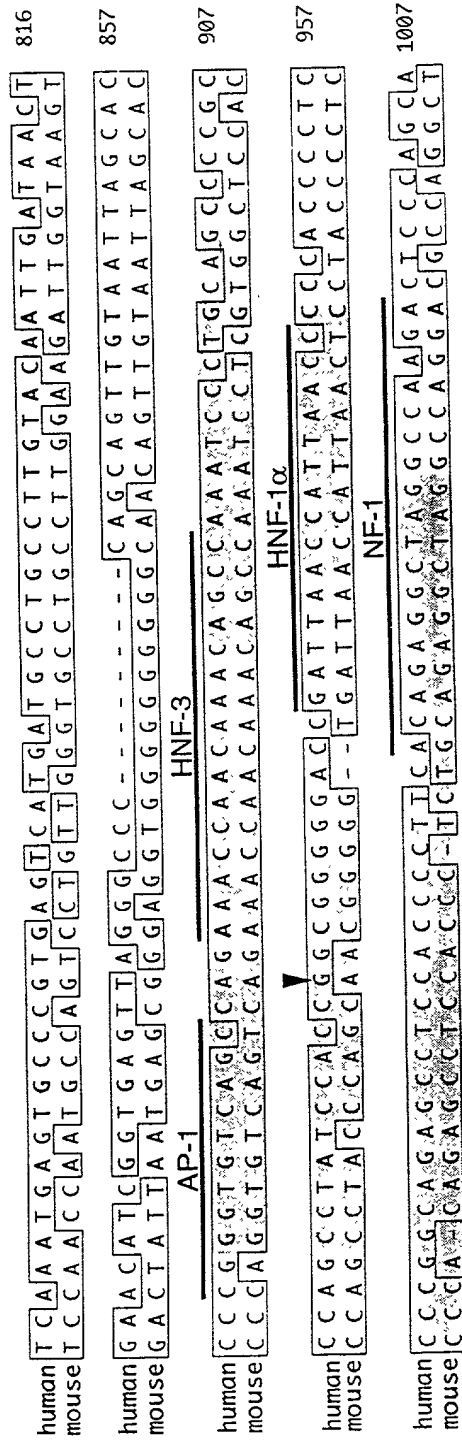


Fig. 13B

human	G A T C T T C C C A G A G G A C G G T T T G A A A G	- - - -	G A A G G C A G A G A G G C A C	- T G	1052
mouse	G A G T C T C C C A G A G G A C A G T T T G A A A G A G A G A G A G A G A G G A C C T G				
human	G G A G G A G G C A G T G G G A G G G C G G A G	- -	G G C G G G G G C C	- - - -	T T C G G
mouse	G G A G G A G G C A G A G G A G G G C G G G A C G G G G G G C T G G G C T C A G C C A G				1091
human	G G - - - T G G C G - - - C C C A G G - - -	G T A G G G C A G G T G G C C	G C G G C G T G G A	1130	
mouse	G G G C T T G G G T G G C A T C C T G G C C G G G C A G G A C A G G G G G C T A A G G C G T G G G				
human	G C A G G G A G A A T G C G A C T C T C C A A A C C C C T C G T C G A C A T G A C A T G				1176
mouse	T A - G G G A G A A T G C G A C T C T C T A A A C C C C T T G C C G G C A T G G A T A T G				

Fig. 13C

125	126	127	128	129
G C G G	G A C	C G G	A T C	A G C A
Arg	Asp	Arg	Ile	Ser

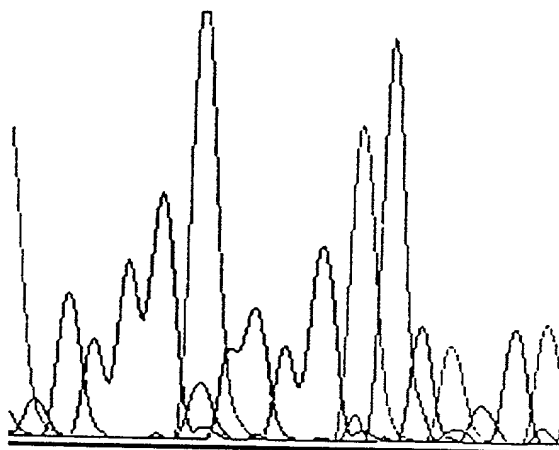


Fig. 14A

G C G G G A C T G G A T C A G C A
Trp

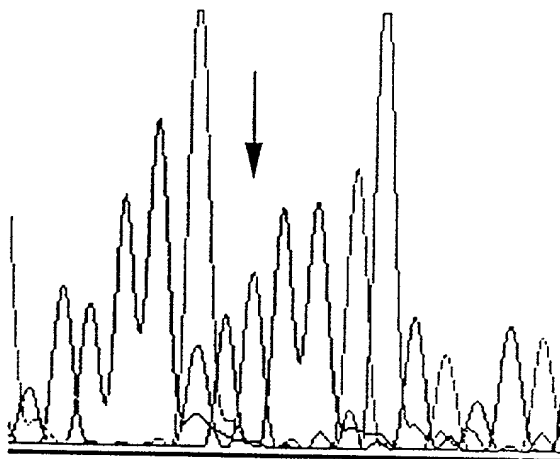
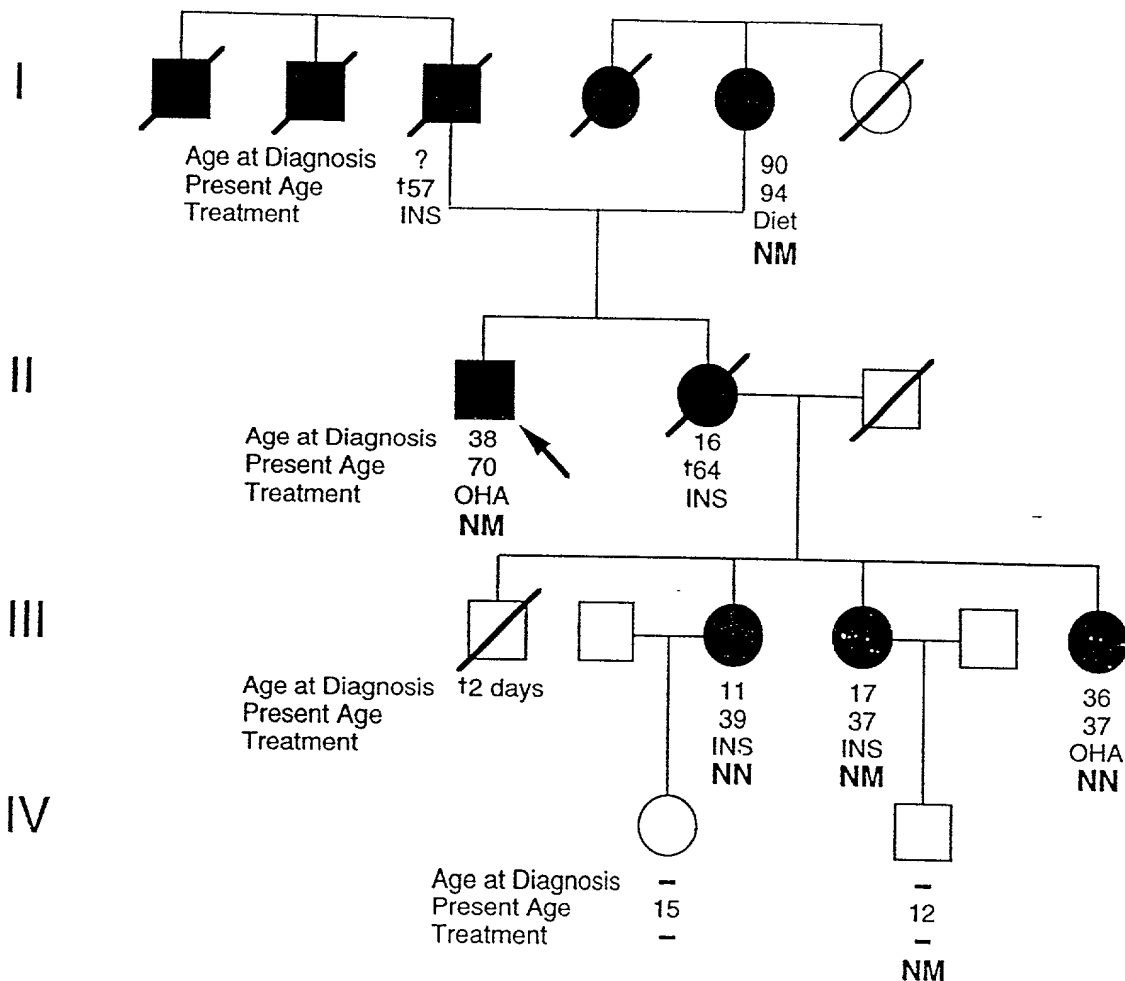


Fig. 14B

[illegible]

J2-21



J2-96

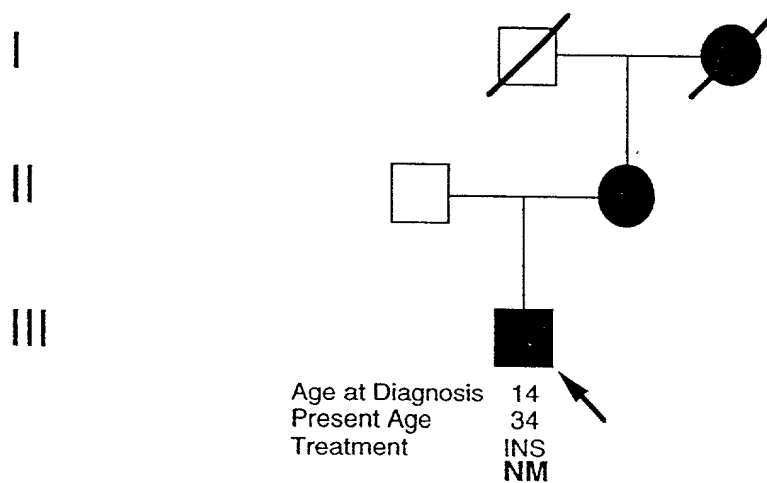


Fig. 15

Fig. 16

I

Age at Diagnosis
Present Age
Present Therapy
Complications

D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424

44 years
64 years
Insulin
R, M, N

8	2	8	4
6	6	1	6
3	1	3	3
M	N	N	N
1	6	9	10
6	1	1	8
5	15	8	10

II

Age at Diagnosis
Present Age
Present Therapy
Complications

D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424

28 years
47 years
OHA

41 years

18 years
37 years
Insulin
R

25 years
33 years
OHA

1	8	4	8	8	8	8
6	6	6	6	6	6	1
3	3	3	3	3	3	3
N	M	N	N	N	M	N
3	1	10	5	7	1	9
2	6	8	4	4	6	1
6	5	10	14	11	5	8

III

Age at Diagnosis
Present Age
Present Therapy
Complications

D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424

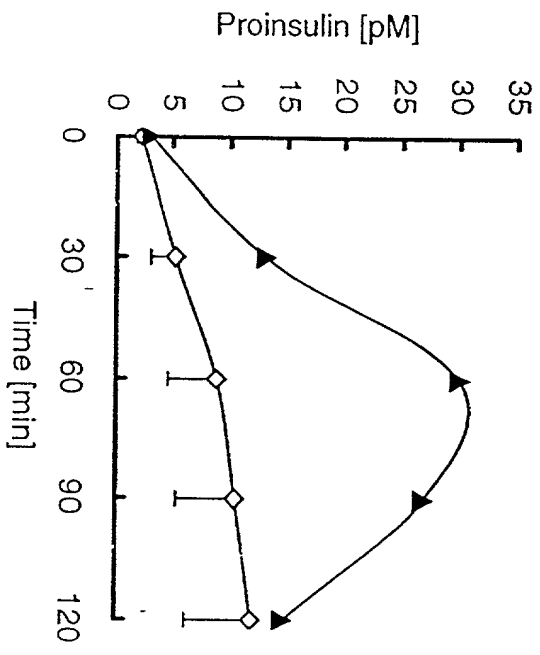
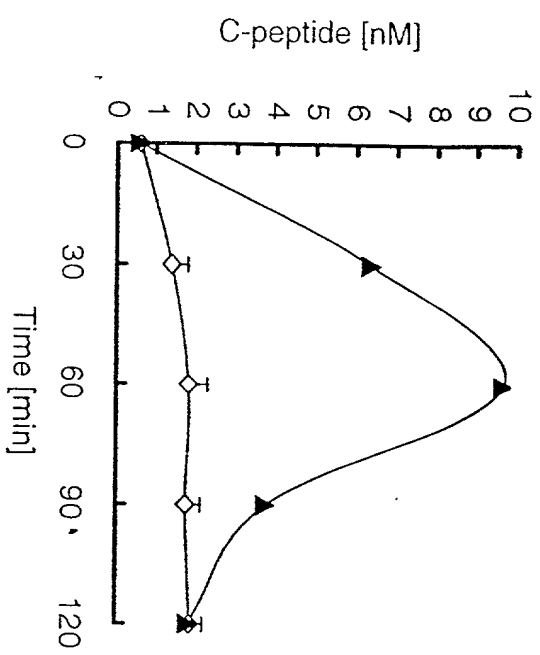
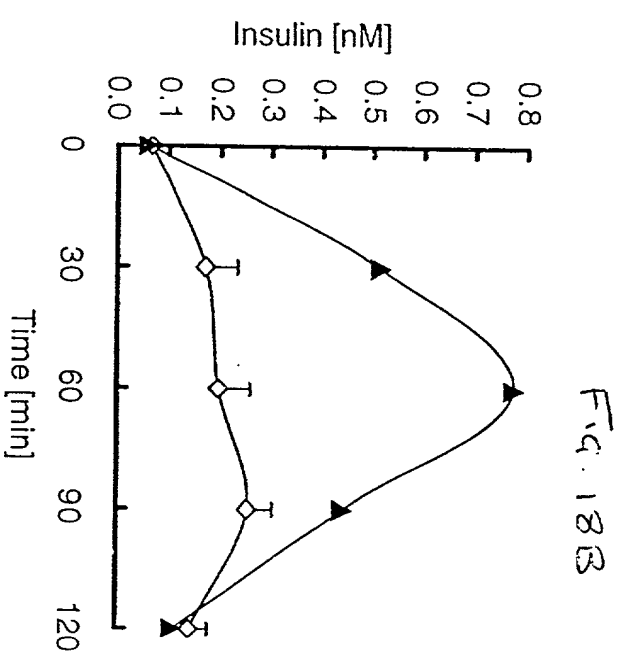
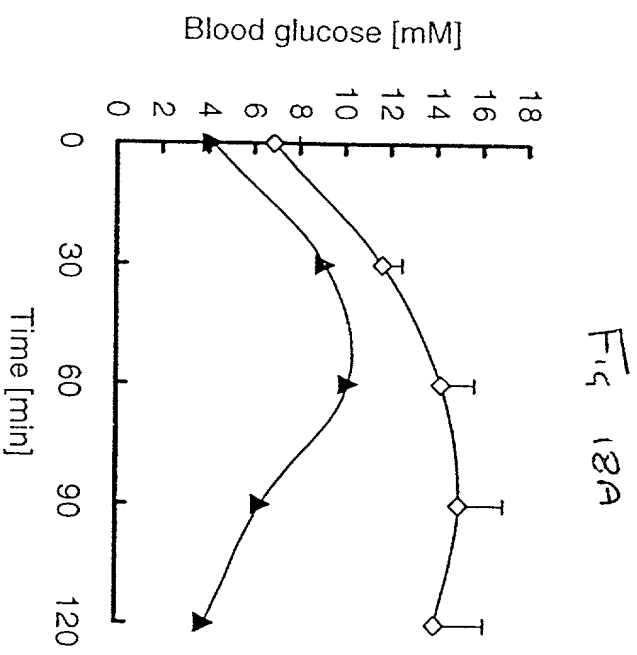
17 years
18 years
OHA

14 years
14 years

8	1	8	8
6	6	6	6
3	3	3	3
M	N	M	N
1	3	1	7
6	2	6	4
5	6	5	11

Ala Glu Val Leu Ser Arg Gln |
Stop
G C G G A G G T C C T G T C C C G A C A G G T A C C G G G G

Fig. 17



09754106-010301

Fig. 19A

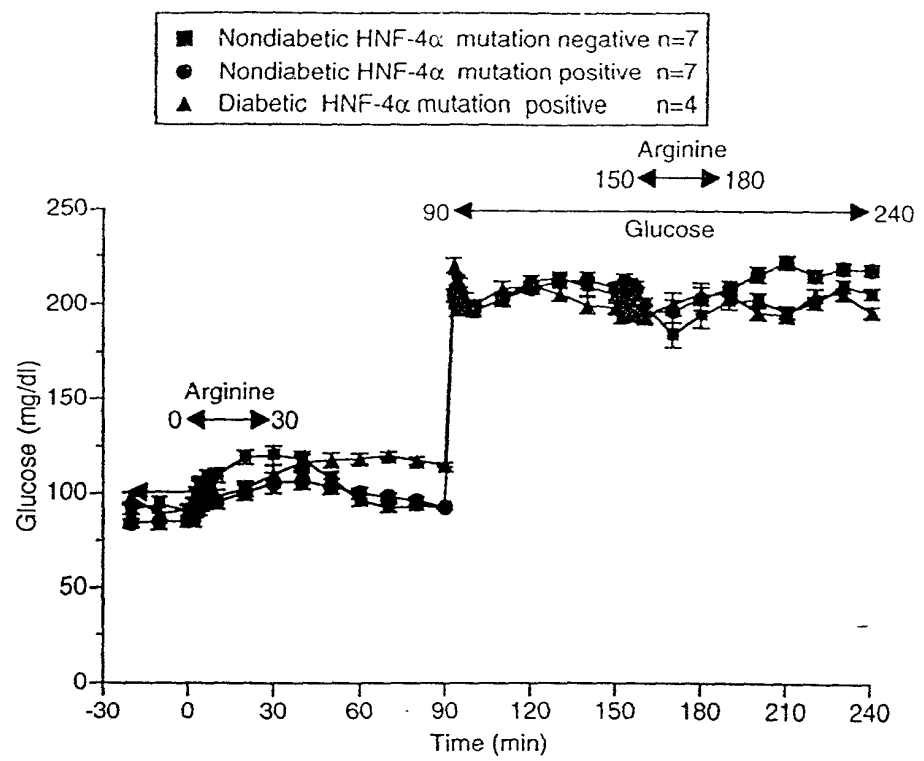
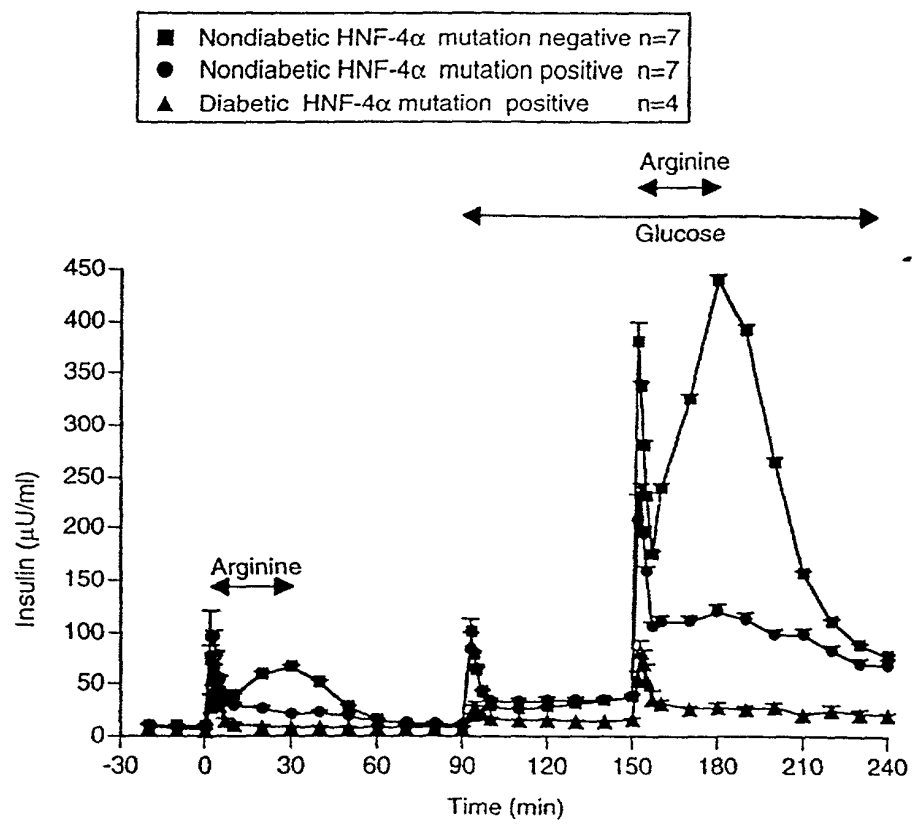
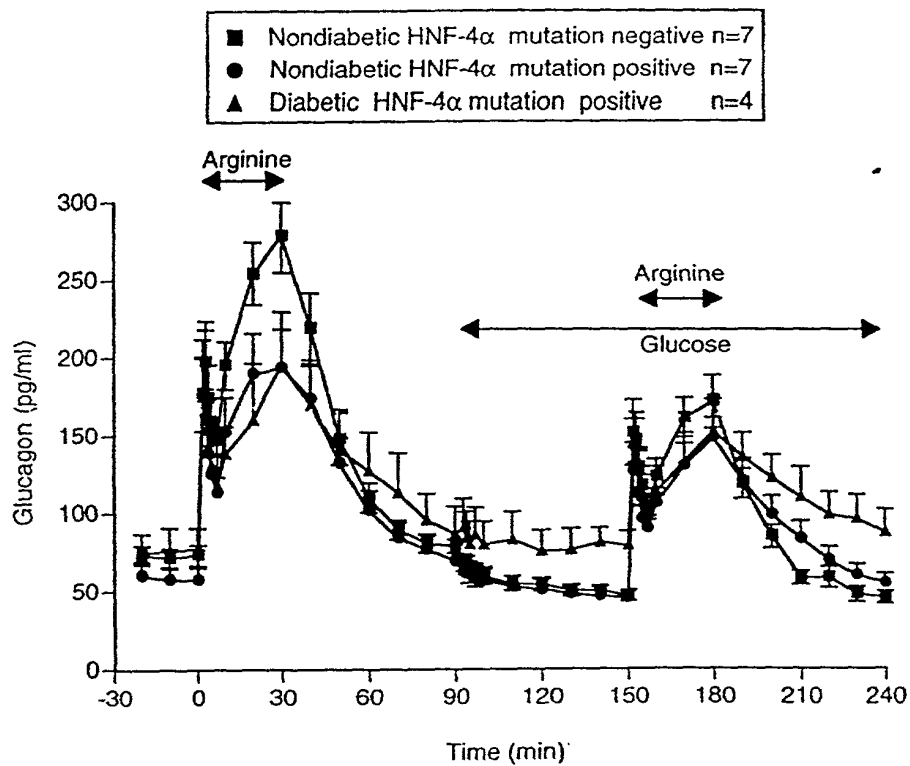
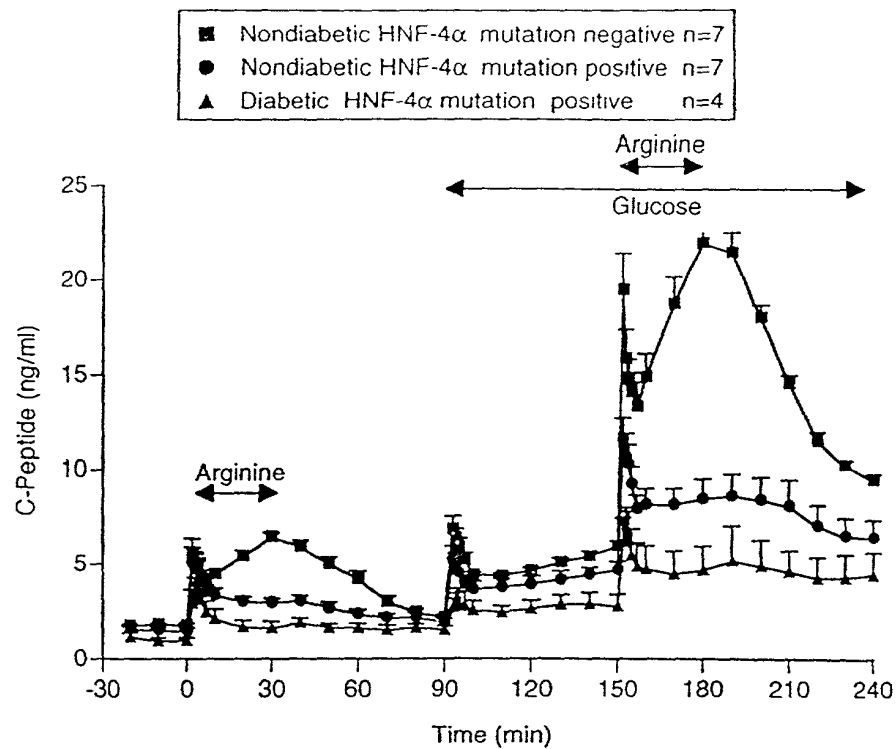


Fig. 19B



[illegible]

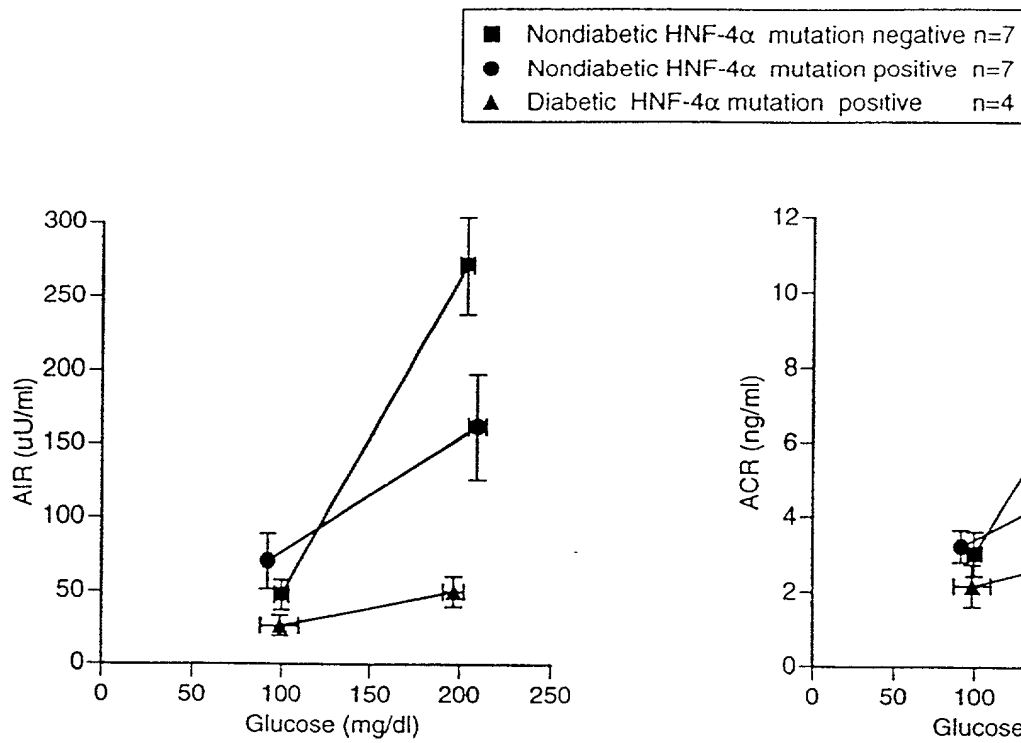


Fig. 20A

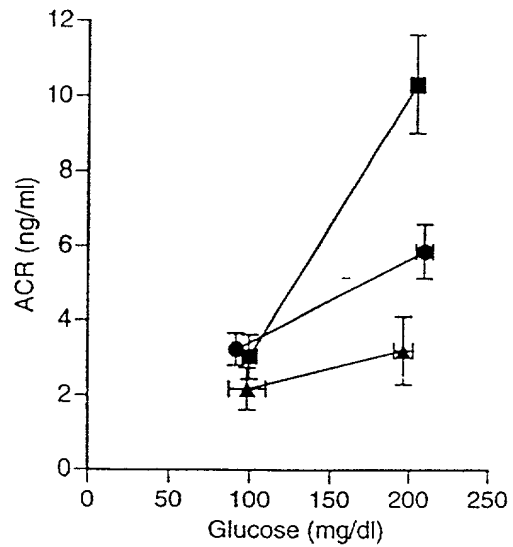


Fig. 20B

11



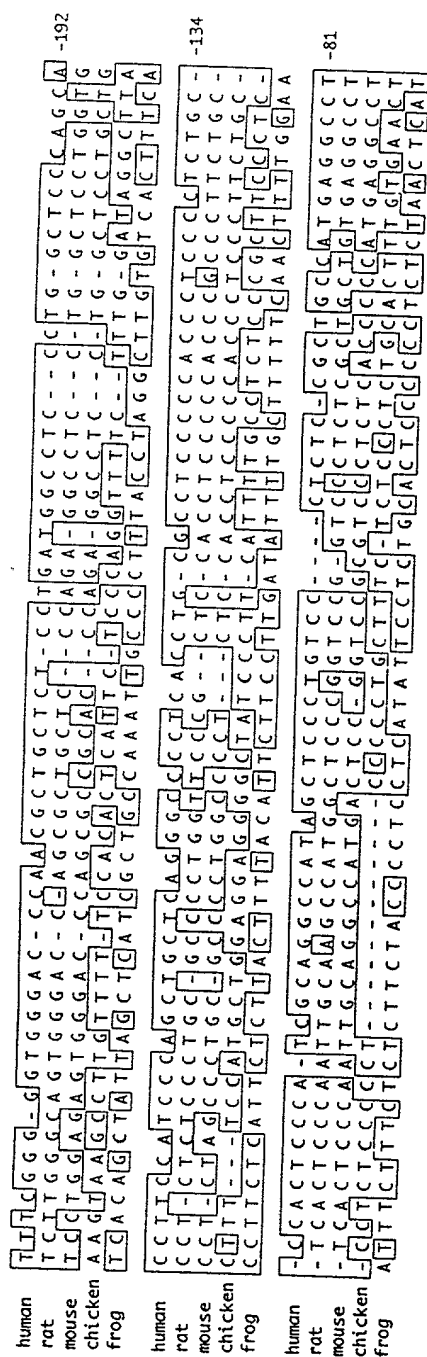


Fig. 22A

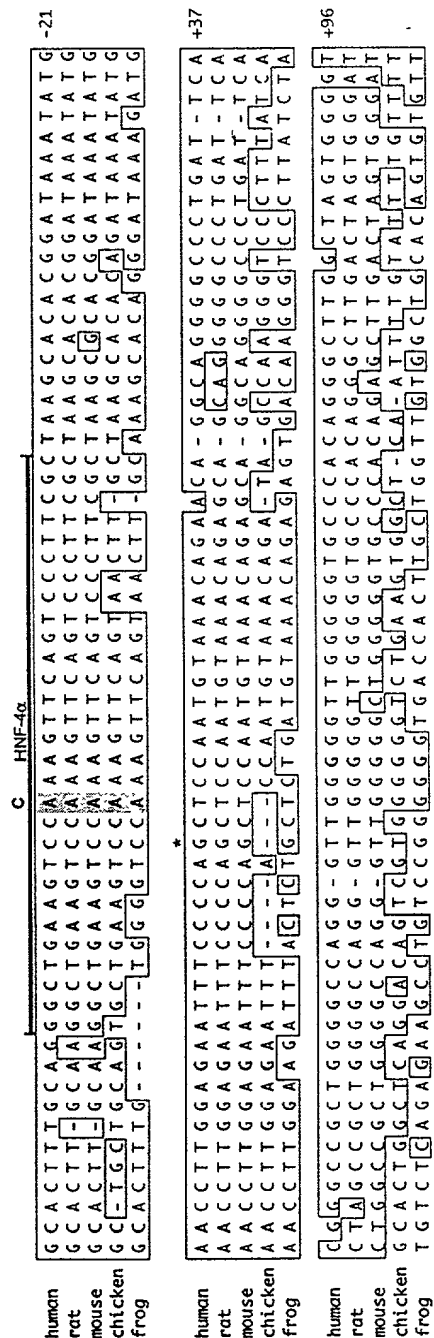


Fig. 22B

Fig. 22C

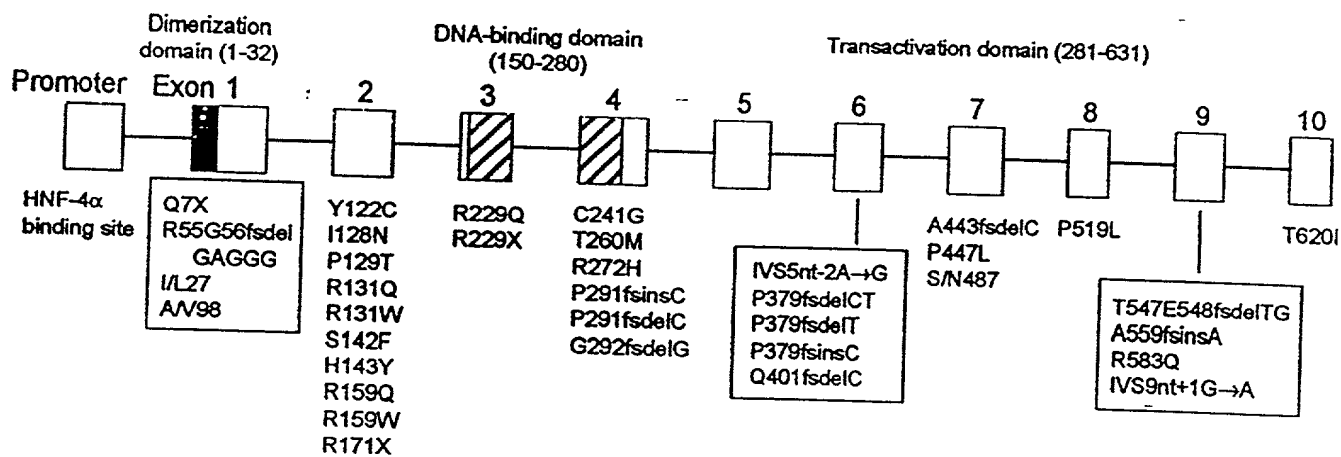


Fig. 23

J2-20

175	176	177	178		
A	AAG	CAA	NGA	GAG	AT
	K	Q	R	E	
			X		
			C/T		

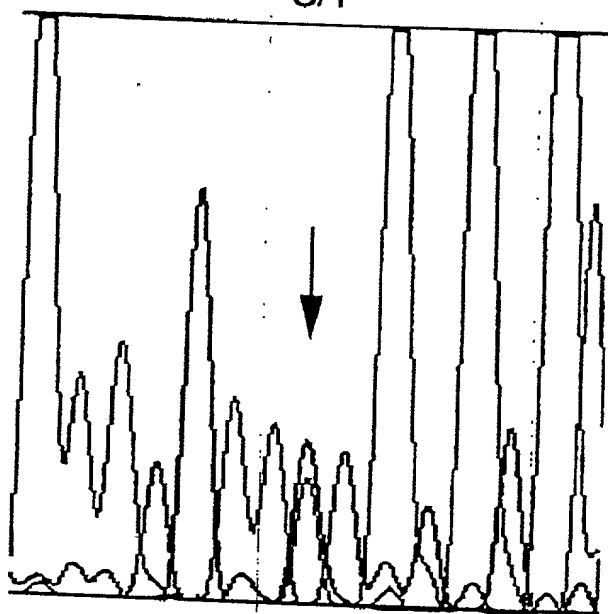


Fig. 24

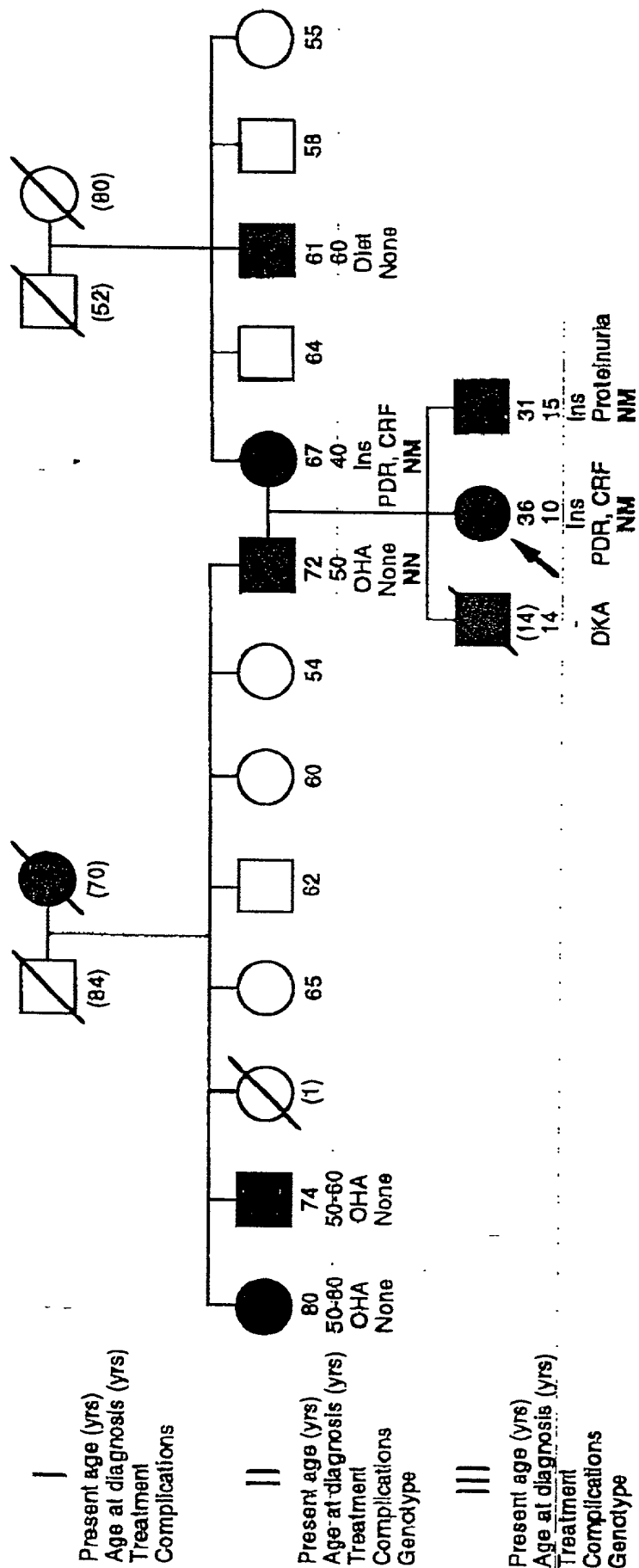


Fig. 25

1 AGCCAGCACGTGTTCTTGGCACATGGTAATCTTAACATATTTTTTCTACAGGAGGCCCTGGTGTCAAGCCGGGAGTGGGGTGGAAAGGTC
 NF1 HNF-3 AP1
 91 CCAAAATGGATGGAAGGGCCCCAAATGGCGGTGAGCATCCCTCTGCCCTTGAGAAAGAGCTAGCCCAAGCTGTCTAGAGCTCCCTGGCTGCTG
 NF1 AP4
 181 CCGCTCTCGTAAGCAGCAAGCAATTTTGGCTCTCCTGTCTCAGCATGATGCCCTTACAAAGTTCTTTTCGGGGGTGGGACCCAAACGCTGCT
 NF1 AP4
 271 CTCCTGATGGCCTCCCTGGCTCCAGCACCCCTTCCATCCAGCTGCTCAGGGCCCCCTCACCTGCGCCTCCCCCAACCTCCCCCTCTGCCCCAC
 NF1 AP4
 361 TCCCATCGCAGGCCATAGCTCCCTGTCCCTCTCCGCTGCCATGAGGCCCTGCACCTTTGCAAGGCTGAAAGTCCCAAGTTCAAGTCCCTTCGCT
 HNF-3 C/EBP * Exon 1 HNF-3 AP1
 451 AAGCACACGGATAAATATGAACCTTGGAGAAATTTCCCCAGCTCCCAATGTAAACAGAACAGGCAGGGGCCCTGATTCAAGGGCCCGCTGGGG
 541 CCAGGGTTGGGGTTGGGGTGCCACAGGGCTTGGCTAGTGGGGTTTGGGGGGGCGAGTGGGTGCAGGAGTTTGGTTTGTCTGCTGCCG

FIG. 26A

631 GCCGCGAGGCAACGCAACCCACGCGGTGGGGGAGCGGCTAGCGTGGTGGACCCGGCGCGGTGGCCCTGTGGCAGCCGAGCCATGGTT^{MetVal}
 SerLysLeuSerGlnLeuGlnThrGluLeuLeuAlaLeuAlaLeuLeuGluSerGlyLeuSerLysGluAlaLeuIleGlnAlaLeuGlyGlu^{Leu}
 721 TCTAAACTGAGCCAGCTGCAGACGGAGCTCCTGGCGGCCCTGCTCGAGTCAGGGCTGAGCAAAAGAGGCACTGATCCAGGCACTGGGTGAG^G
 ProGlyProTyrLeuLeuAlaGlyGluGlyProLeuAspLysGlyGluSerCysGlyGlyGlyArgGlyGluLeuAlaGluLeuProAsn
 811 CCGGGGCCCTACCTCCTGGCTGGAGAGGCCCCCTGGACAAAGGGGAGTCTCGCGCGCGGTTCGAGGGGAGCTGGCTGAGCTGCCCAAT
 GlyLeuGlyGluThrArgGlySerGluAspGluThrAspAspGlyGluAspPheThrProProIleLeuLysGluLeuGluAsnLeu^{Val}
 901 GGGCTGGGGGAGACTCGGGGCTCCGAGACGAGACGATGGGAAGACTTCACGCCACCCATCCTCAAAGAGCTGGAGAACCTC
 SerProGluGluAlaAlaHisGlnLysAlaValGluThrLeuLeuGln(n)109
 991 AGCCCTGAGGAGGGGGCCACCAGAAAGCCCGTGGTGGAGACCCTTCTGCA gtaaggagccctgccccgtccccgagagagccta^T

FIG. 26B

ac

1801 MetValLysSerTyrLeuGlnGlnHisAsnIleProGlnArgGluValValAspThrThrGlyLeuAsnGlnSerHisLeuSerGlnHis
 ATGCTCAAGTCCTACCTGCAGCAGCACACATCCCACAGCGGGAGGTGGTCGATACCACTGGCCCTCAACCAAGTCCCACCTGTCCCCAACAC
 A (R131Q)
 1891 LeuAsnLysGlyThrProMetLysThrGlnLysArgAlaAlaLeuTyrThrTrpTyrValArgLysGlnArgGluValAlaGlnG (ln) 176
 CTCACACAGGGCACTCCCATGAAGACGACAGAGCGGCCGCCCTGTACACCTGGTACGTCGCCAAGCAGCGAGAGGTGGCGCAGC gtaag
 1981 taatgaccctacccccgcattctccctggaggggccccaggactctccccctaactcataggtgggggctgggaagcttcaccatccccattac
 2071 acagacaggtagatggaaaggaagtcagtgaggattcaacctgcattttattacattattctgcgccaggcactctgtgggacgggagtanac
 2161 ttggtcctgaacatccaaagatgaatgaaatgggtccctgctttcttttttttagata::::: 3.8 kb :::::cgtagact
 2251 ctggaaaaatatgtaagctctctgagcctcagcttcttctcatctgtacaaatgggggagtagtaaaatgtgcaaaatcagaacaaatgctaatgc
 2341 ttacctgcagtcctgtactgagaaggatggtgagatcatatctctgggttgtaggaagcatttcaggagattgattagtgattgttgcctt

FIG. 26D

2431	gaacacaggttaagaaagtgatggcatgtgtgtgtgttctgtcatcagtagatttctaagttcttagctgtaagctcctct
2521	ggttcagcgccatggcaatgagaaagaatcaaggccaaggtcagggaatggacaggaaggtgagagtggccagtagcccaactcacgg
2611	Exon 3 176 (g)lnPheThrHisAlaGlyGlnGlyGlyLeuIleGluGluProThrGlyAspGluLeuProThrLysLysGlyArg ctttctgtgcctgcag AGTTACCCATGCAGGCAGGGAGGGCTGATTGAAGAGCCACAGGTGATGAGCTACCAACCAAGAGGGGCGG
2701	ArgAsnArgPheLysTrpGlyProAlaserGlnGlnIleLeuPheGlnAlaTyrgluArgGlnLysAsnProSerLysGluGluArgGlu AGGAACCGTTCAAGTGGGGCCAGCATCCAGCAGATCCTGTTCAGGCCATGATGAGAGCGCAGAGAACCCTAGCAAGGAGGACCGAGAG
2791	ThrLeuValGluGluCysAsnAr (g) ²³⁸ ACGCTAGTGGAGGAGTCAATAG gtacaacggcggcgcggaacagtgctgtgttggctcggcgaagggccaggggaaggggaag

FIG. 26E

2881 gtgactctaggtcctgtaaaaggctgtccagttg^cccgagaactcctgatattggcttagcctgcccagaaaaattgagaataacttgaacc

2971 taagcccatctctcgagccccccctgcacntggacaccaagcaacccctccatggatgctcacccaattogattctctctacaatcct

3061 atggctcttttgcctcaactttatgaatggagagactgaggtcagacagactgtcaattgcccgaaggtcacacacagacacctggcattggaa

3151 cccagatctgccagcctcaaacctccggcagagntcagcttctcagaacctcccccttcattgccacaggacaggggttcctctgagcctgg

3241 cctggaggctcatgggtggctatttctgcag GCGGAAATGCATCCAGAGGGGTGCCCCATCACAGGCACAGGGCTGGGCTCCCAACC
Exon 4 238 (Ar)gAlaGluCysIleGlnArgGlyValSerProSerGlnAlaGlnGlyLeuGlySerAsnL
G(C241G)

3331 euValThrGluValArgValTyrAsnTrpPheAlaAsnArgArgLysGluAlaPheArgHisLysLeuAlaMetAspThrTyrSerG
 TCGTCACGAGTGGTGTCTACAACTGGTTTGCCAAACCGCGGCAAGAGAGCTTCCGGGCACAAGCTGGCCCATGGACACGTACAGCG
A(R272H)

FIG. 26F

3421 lyProProGlyProGlyProAlaLeuProAlaHisSerSerProGlyLeuProProAlaLeuSerProSerLysValH
 GGCCCCCCCCAGGCCAGGCCGGACCTGCGCTGCGCTCACAGCICCCCTGGCTGCTCCACCTGCCCTCTCCCCCAGTAAGGTCC
 C (P291fsinsC)
 isG(1Y) 319
 3511 ACG gtaagtgtatgtggggacacacgtgggaagtgaggaggttggggaggactgtccattgacagcagtcacctaaccctct
 3601 ttgcacgtcagtttggttccattc::: 2 kb ::::gcagctgacccagggttagcaaaaggtagaaacaaaggcagattt
 3691 gctggctgcataaaggcagacaggcagatggcctaagcaaaccaatggagtttgaagtgtctgagggtctgtggaggcaggggagggcaggg
 Exon 5 319 (G)lyValArgTyrGlyGlnProAlaThrSerGluThrAlaGluValProSerS
 3781 aagtgggtgtctgaggcagcagactgcttccctctccag GTGTCGCTATGGACAGCCTGCGACCACTGAGACTGCAGAGTACCTCAA
 erSerGlyGlyProLeuValThrValSerThrProLeuHisGlnValSerProThrGlyLeuGluProSerHisSerLeuLeuSerThrG
 3871 GCAGCGCGGTCCCTTAGTGACAGTGTCTACACCCCTCCACCAAGTGTCCCCCACGGGCTGGAGCCCCAGCCACAGCCTGCTGAGTACAG

FIG. 26G

3961 luAlaLysLeu³⁶⁹
 AAGCAAGCTG gtgagtgtccttgctgtaaggaaacccaacctcatcttccctggcaggagattctggagcagtccttagggaggc
 4051 cctgtgggacccccggcccccgacacagcttggtctccctcgtag GTCTCAGCAGCTGGGGGCCCTCCCCCTGTCTCAGCACCCCTG
 ThrAlaLeuHisSerLeuGluGlnThrSerProGlyLeuAsnGlnGlnProGlnAsnLeuIleMetAlaSerLeuProGlyValMetThr
 4141 ACAGCACTGCACAGCTTGGAGCAGACATCCCCAGGCCCTCAACCCAGCAGCCCCCAGACCTCATCATGGCCTCACTTCCTGGGGGTATGACC
 (P379fsdelCT)
 (IVSnt-2A-G)
 (Q401fsdelC)

FIG. 26H

IleGlyProGlyGluProAlaSerLeuGlyProThrPheThrAsnThrGlyAlaSerThrLeuValIleG(ly)⁴³⁷
4231 ATCGGCGCTGGTGAGCCTGCCTCCCTGGGTCTACGTTCCACACAGGTGCTCCACCTGGTCATCG gtaagctggtggggatgggt
4321 gggcacctgggtgggaggctcatggggcaaccgcanaatccaggagctggaaaagccactgggactcattcattcattcattc
4411 caacatgt::::: 0.8 kb :::::taggagaggggagcagagaactgaccccatggcctttgcaactgctgtggtaccccccagggtc
4501 cagggaaccgcagtttgacaacttttgacaagtccaccgcttgcttttccattagcttagacaaagagctaaaggctcagagaggggga

Figure 1 continues on the next page

DIABETES, VOL. 46, MARCH 1997

331

FIG. 26I

FIG. 26J

lnSerProHisA (la)⁵⁰¹
 4951 AGAGCCCCACG gtgagcaccctgtgccccacacagcaggagatgatgatagaggttggtgtcaa tggatgcaggggaagggtgcct
 5041 ggcaggcattgcagtctgcattgtctctgggacaagtgtgtttccgtgattgaggggtgtctgcaggccagtggttcccatgtgaatgc
 5131 acgtatctgtgtgtgcacgactgtgtgtgagcagatccctagtgcgtgtctgggtgtgtatcggttgcatttgggtgcatt
 5221 gcctgtgtttctctgaaactcttagggcccatatgaatttctaaaaatctattcaga:::: 1.5 kb ::::ccagttttgaaaaatc
 5311 agccttgggatctccaactgctgcccagtcctgggtgttcagcaggcccccatgccccctttccccagtccttgaggcctgggactagggtg

FIG. 26K

eGlnHisLeuGlnProAlaHisArgLeuSerAlaSerProThrV(al) 590
 5761 CCAGCACCTGCAGCCGCCACCCGGCTCAGCGCCAGCCCCACAG **a(IVS9nt10-A)** gtgagaggccctggctccacccccctcccttactgtccctgccccct
 5851 tccatgttggtcccccccccttctgtgtgctccgtcactgtgggctgtgcatgcagcagccctagggtgctgtgaggaagcactggca
 5941 ggcgtggaagggtgggtggcttccatgaa::: 1.5 kb ::::: tccagtgttcacagtaagatgtactcagggccagtcctcatgg
 6031 gcggccgtggaccctggctgggaggctccctttgttaagaaccagaggttagaggtgtgactttgggttccctgttatgtgctgtgatcca
 6121 ggaggtgtggccctgcctccccatcctgagtaccctagggaacaggcagggtgggtgtgggtgcctggtgggtgggtgtagcagcctt

Exon 10 590 (V) alSerSerSerSerLeuValLeuTyrGlnSerSerAspSerSerAsnGlyGlnSerHisLeuLeuProSerAsnHi
 6211 gtttgccctctgcag TGTCTCTCCAGCAGCCTGGTGTACCCAGAGCTCAGACTCCAGCAATGGCCACAGCCACCTGCTGCCATCCCAACCA
 sSerValIleGluThrPheIleSerThrGlnMetAlaSerSerSerGlnOc⁶³¹
 6301 CAGCGTCATCGAGACCTTCATCTCCACCCAGATGGCCTCTTCCTCCCAGTAACCCACGGCACCTGGGCCCTGGGGCCTGTACTGCCCTGCTT
 6391 GGGGGGT

FIG. 26M

PrF
CATGAACCCGGAAGAGTAGTCTCTCTGGACTAAAGCGGAACGTAGAACCCCGCGCTAGGCTGCAAGCACTGGCTTAACAAGTCCAAAAGTTAGGTGAAGTTT
GGCTGATAAGCAGAACCAAGTAAAGAGGTCTCTAGCCCCCAGCGTGAATGACCTGGCAAGCCCGCTCCCGCCAGGTCTTCTGCTCTCCAGGTCTGCCCTCCCGCTCT
CCCTCTCTCCGGGTTTCCCTCCCTCCACCATCATTTGATCCAGCGAAAGCTGGCCCTTCCCACTAATTGTCATATCTTATGCGCTAATGCTGGCATCATGGCAAGTT AGAAG
Exon 1
TTTTCTGACTCCTTTCCGGAGGAGCTCCCGGACCCCGGGGAGTACAGGTCTGTGGAGCTGAGGGTTCCTGGATTGCGGTTTGGCTTGTGAACCTCCCTCCACCTCCTC
PrR
TCTGCCACCCACCCCTCACCCCTTCTTTTTCGTCCTTGAAA
Met Val Ser Lys Leu Thr Ser Leu Gln Gln Leu Leu Ser Ala Leu Leu
ATG GTG TCC AAG CTC ACG TCG CTC CAG CAA GAA CTC CTG AGC GCC CTG CTG
Ser Ser Gly Val Thr Lys Glu Val Leu Val Gln Ala Leu Glu Glu Leu Leu Pro Ser Pro Asn Phe Gly Val Lys Leu Glu Thr Leu Pro
AGC TCC GGG GTC ACC AAG GAG GTG CTG GTT CAG GCC TTG GAG GAG CTG TTG CTG CCA TCC CCG AAC TTC GGG GTG AAG CTG GAG ACG CTG CCC
Leu Ser Pro Gly Ser Gly Ala Glu Pro Asp Thr Lys Pro Val Phe His Thr Leu Thr Asn Gly His Ala Lys Gly Arg Leu Ser Gly Asp
CTG TCC CCT GGC AGC GGC GGC GAG CCC GAG ACC AAG CCG GTC TTC CAT ACT CTC ACC AAC GGC CAC GCC AAG GGC CGC TTG TCC GGC GAC

FIG. 27A

Glu Gly Ser Glu Asp Gly Asp Tyr Asp Thr Pro Pro Ile Leu Lys Glu Leu Gln Ala Leu Asn Thr Glu Glu Ala Ala Glu Gln Arg
GAG GGC TCC GAG GAG GGC GAC GAC TAT GAC ACA CCT CCC ATC CTC AAG GAG CTG CAG GCG CTC AAC ACC GAG GAG GCG GCG GAG CAG CGG
115
Ala Glu Val Asp Arg Met Leu Ser(r)
GCG GAG GTG GAC CCG ATG CTC AG GTAGGCGCAGAGCCAGGTGGAGGGGACCCACCCGAGCCCTGGAGCCCCCGGGCCCTGAGTACACTGCGCCCCGACACACTCGCC
Ex1-2R
AAGCCCGTTTCCCAACCAAAAATTCCCGCGGGGCGCTCTCTCTCCCAACACCCGAGCCCTTCCCAATCCCTTAGGGGACAAACCCCTGGCGCCCAACCGGGCTTCTTCTCCCGAGGC
CCAGGCCATCGTCC: 9 kb : : : : : TCAGAGAGAGGGATGAGGTGTACCGTACAGGGGCGAGTCACCTTCTCTCTGTGTAGCTTCCATTTTGGCCCTCATGTCTACCCCAAA
115
GTGTAGCTTAGATGGGGGAAAATTCAGAAATTTGCGATAGACCATAGGTAGACCCCTAGAAAAAGAAATGTTTCTCCCGAGATGCTCTCCCACTAGTACCTAACCACTCTGCTTGTCTGT
2 (Se)r Glu Asp Pro Trp Arg Ala Ala Lys Met Ile Lys Gly Tyr Met Gln Gln His Asn Ile Pro Gln Arg Glu Val Val Asp Val Thr
CTAG T GAG GAC CCT TGG AGG GCT GCT AAA ATG ATC AAG GGT TAC ATG CAG CAA CAC AAC ATC CCC CAG AGG GAG GTG GAT GTC ACC
Gly Leu Asn Gln Ser His Leu Ser Gln His Leu Asn Lys Lys Thr Pro Met Lys Thr Gln Lys Arg Ala Ala Leu Tyr Thr Trp Tyr Val
GGC CTG AAC CAG TCG CAC CTC TCC CAG CAT CTC AAC AAG GGC ACC CCT ATG AAG ACC CAG AAG CGT GCC GCT CTG TAC ACC TGG TAC GTC
182
Arg Lys Gln Arg Glu Ile Leu Arg G(1n)
AGA AAG CAA CGA GAG ATC CTC CGA C GTAAGTGTTCATCTGCTCTGCTCTGCTCAACCTGAAGTGACCTTTGCGCCCTCTCACCCCATTTGGCTGCTCAGTTTCCCTTTTCATCGAC
Ex2R

FIG. 27B

[illegible]

Met Arg Arg Asn Arg Phe Lys Trp Gly Pro Ala Ser Gln Gln Ile Leu Tyr Gln Ala Tyr Asp Arg Gln Lys Asn Pro Ser Lys Glu Glu
 ATG CGC CGC AAC CGG TTC AAA TGG GGG CCC GCG TCC CAG CAA ATC TTG TAC CAG GCC TAC GAT CGG CAA AAG AAC CCC AGC AAG GAA GAG
 270
 Arg Glu Ala Leu Val Glu Glu Cys Asn Ar(g)
 AGA GAG GCC TTA GTG GAG GAA TGC AAC AG GTAACACACACAGAGCTCAGTGGGAGGTCACACAGACCCAGAACCCCTCCCTCGGTCCTGGGATATTGAGA
 EX3R
 CACTAGTTATACAGATAAGTGTGGCTAAATCAGAGCTTCTCAAGTATGTCCACA::: 2 kb :::::CTGATTGTGTGTTTTTGGGCCAAGCACCAACAAGTCCCGCGCCCC
 EX4-1F
 270
 Exon 4 (Ar)g Ala Glu Cys Leu Gln Arg Gly Val Ser Pro Ser Lys Ala His Gly Leu Gly Ser Asn Leu Val
 CCTTCACTACCATCTCCCTCCATCCATCCATCCAG G GCA GAA TGT TTG CAG CGA GGG GTG TCC CCC TCC AAA GCC CAC GGC CTG GGC TCC AAC TTG GTC
 EX4-2F
 Thr Glu Val Arg Val Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu Glu Ala Phe Arg Gln Lys Leu Ala Met Asp Ala Tyr Ser, Ser Asn
 ACT GAG GTC CGT GTC TAC AAC TGG TTT GCA AAC CGC AGG AAG GAG GAG GCA TTC CGG CAA AAG CTG GCC ATG GAC GCC TAT AGC TCC AAC
 349
 Gln Thr His Ser Leu Asn Pro Leu Leu Ser His Gly Ser Pro His Gln Pro Ser Ser Ser Pro Pro Asn Lys Leu Ser G(ly)
 CAG ACT CAC AGC CTG AAC CCT CTG CTC TCC CAC GGC TCC CCC CAC CAG CAG CCC AGC TCC TCT CCT CCA AAC AAG CTG TCA G GTAAGCAAAGGT
 G K Q R

FIG. 27D

EX4-1R

TGGGCGCTCACGCTCGGCAACCCAAACATCCTGGTCTGCCACGGATCTATCTGGTCTTACAGAGGACAAACGCTTTTACAGATGATCCTAGGCGCGCTCTCTCATTTGCCA
L G L T A S A T Q P S W F L P R I L S G L R V F R G A N A F E M I L G P L S H C Q

GAATATACTCCCTCGGAATAATGTGTGGCTCTGATCAGTTT::: 3 kb ::::CCAAAGCACTGGGGATCATCATGTGAACAAACAGAGATAAAAAATTTCTTGGCCCTCGTG
N I L P W K OC

399 K C

CGCCTTACATTTCTAGAAATTAAATAGAGAACATGCCATATTTTACCCTGGAGAAAAGCAGCCGATATTTCTTGTGGTGGAGGAGCAAGCAACTTTATTTTCTTTATTTACCCACCCCT

349

35X3

TGAACACAGAGGTGCCAGCATTGTTCCAGGACCCCTGGTGGCACTAATGTGCCCTACTGGGTGTGTGCTTTTTCAG
 Exon 5 (G)ly Val Arg Tyr Ser Gln Gln Gly Asn Asn
 EX5F

Glu Ile Thr Ser Ser Thr Ile Ser His His Gly Asn Ser Ala Met Val Thr Ser Gln Ser Val Leu Gln Val Ser Pro Ala Ser
GAG ATC ACT TCC TCC TCA ACA ATC CAC CAT GGC AAC AGC AGC GCC ATG GTG ACC AGC CAG TCG GTT TTA CAG CAA GTC TCC CCA GCC AGC

402

Leu Asp Pro Gly His Asn Leu Leu Ser Pro Asp Gly Lys Met

EX5R

CTG GAC CCA GGC CAC AAT CTC CTT TCA CCT GAT GGT AAA ATG GTGAGTACACCTGGGCCATTGTCGCTTGGAGCTGATAAGATAAGAGCGCAAAACAACAACCTT
CTCAACAGGGCTGCGCTTCAACAATGAAACCAATTGTAGCCCCCATAGGGGAAAATGAGGGCTCTCCAGAGCTCGGAAAGAGAGAGGTAGTCTGTGTGACCCACCCCTTTGGCGGGTAGAAAA:::

... 5 kb ... :CCCAAGTGTGGGATTACAGCGGTGAAGCACCATGCCCGCCAAATAATTGTATTGAGTGAA.TGAAGGAATGAATTTTAGAACAAGTCTATGCCAAGGAATTCGCCTAT

FIG. 27E

403
 EX6F
 AGTCACATCGTTGGAAACTGCTCTTTTGGTCCAAAGTCCACCCATGTTTCTCTTGTGTTTCTCTCCATCAG ATC TCA GTC TCA GGA GGA GGT TTG CCC CCA GTC
 Exon 6 Ile Ser Val Ser Gly Gly Leu Pro Pro Val
 Ser Thr Leu Thr Asn Ile His Ser Leu Ser His Asn Pro Gln Ser Gln Asn Leu Ile Met Thr Pro Leu Ser Gly Val Met Ala
 AGC ACC TTG ACG AAT ATC CAC AGC CTC TCC CAC CAT AAT CCC CAG CAA TCT CAA AAC CTC ATC ATG ACA CCC CTC TCT GGA GTC ATG GCA
 447
 Ile Ala Gln S(er)
 ATT GCA CAA A GTAAGTTCTATTCTTGGTTGGAAACCTGGGGCAGGAGAGAAGAAATTAATGTGTGTAATAAATAACTGTAGGTCTCTTCAAACCTCACCACAAAC
 EX6R
 TAGTAAATTTGGTTTAACTTTAGTTTCTATCTCTCTCTCTTAAATCCCAATATTTGGATTTGTTAGCCCTAAACAAAGAAAATTTGTGGATTTGGATCTCTGGTCACAGTTTACG
 AGCTGTCATCCTGGGTCAAATCATTTGAACCT:.....4 kb :.....ATGACTCTGGGAGACTCTCAGGCTTTTAATCAGATCTGTTTAAATGCCCATCTCCAAACCCACAACCTCATTTG

FIG. 27F

TGGAACTTGAGCAAGTAAATTAATATCTCCCAAGTCTCGGTTTCTTTTACACTTGCCCTCCCATGGAAATCTCTATGTAAACAGGCTCAGCCCGTGACTGGGACATTTAGCGGGGGCTCAAATG
 447
 ATGGCATCCATCCACCTCTCCTTATCCAGGAGCTGTCTGTCTCTTTTCCCTCTCTCCACAG GC CTC AAC ACC TCC CAA GCA CAG AGT GTC CCT GTC ATC AAC
 Exon 7 (S)er Leu Asn Thr Ser Gln Ala Gln Ser Val Pro Val Ile Asn
 Ser Val Ala Gly Ser Leu Ala Ala Leu Gln Pro Val Gln Phe Ser Gln Gln His Ser Pro His Gln Gln Pro Leu Met Gln Gln Ser
 AGT GTG GCC GGC AGC CTG GCA GCC CTG CAG CCC GTC CAG TTC TCC CAG CAG CTG CAC AGC CCT CAC CAG CAG CCC CTC ATG CAG CAG AGC
 512
 Pro Gly Ser His Met Ala Gln Gln Pro Phe Met Ala Ala Val Thr Gln Leu Asn Ser His M(et)
 CCA GGC AGC CAC ATG GCC CAG CAG CCC TTC ATG GCA GCT GTG ACT CAG CTG CAG AAC TCA CAC A GTAAGGACACGGGCATGTGGAGGGAGGGAGCACTCA
 EX7R
 GGACCTCAGTGGCCAACCACTTTCCCTCTCTGGGCTCTGAACCTTCTCGGAAGTTTATTGGCTTGGTCACTTTTCCCTGCTATGATCAACCGACTAGACAAATTTTCTCAAGCATAACTCT
 TGAGTGTGCTGTACCTTTTCTAGTCCCTTCTCTACCCCTGAGATTCCAGGGAAGGTTTGAA: : : : : 2 kb : : : : : TGACCTTTGCTCCCGTTCCGTACCGGAGGCCCTCCCT
 GGTAGGAAATGTGTCTGAGAGCAGGTGGTTCTCCCTCAGAGCCCAAGCATCCACATGCTTTTCGGAGTTGGTTATGTGACTTGGAAATTTACATGAATCTTATGGATAACTAATATAGAGAA
 EX8F
 ATCCCCACTATAACCAACCAAGCCCTTTTATCTACCTGAGGAGATGGGAGCTATGGTGTGGGATGGGGGCTCTGTACCTGTGTCTTTGCCCTGTGTATGCACCTTGATTCTGTCTTCACTCTGT

FIG. 27G

GCGGAAAGCCAGTTCCCTCTATGCAATATGCCCAATGCGCTCTCCACAGATGTCAAGGACTCCTGTCTGTGGAGTGGGACACAAAGGAACCCGAGAGAGCAAGAAAGCC
 GTACTGTCTATGTTGTGATCCTTCATCGAACAACACTGATGCGAATACTTGAACTCTGTACTGAAATGAGGAGAGAGGACATGTGCTATTGAACTGAGGCCAAACACACTGTAAATATCCAC
 AGACTCCCTCCCTGCCCCATFCCACATGATCTTTGAGATTTCTTTTAAAGAAATTTTGTCCAAATGGCTGTAAACTATAAACTACTGTAAATTAAGTGCAATTTCCCTCTGTGTCTC
 TCCCTCTGCCCCGTGTATATAATACTAAAGTGTCTATTAGTTTCTTTGTAAAGTCAGAGTCAAAATTTCAAAAGTGTCTCTCCCTCTCAAGGAAACATCCCTAAAGTGGAAAG
 TGAAGCCCCCTTGTCTCTCCCGGGGCTGGACACTTATGGGACAGCATACCTTGGACTGACTACAGCTTAACCTCCAGTCTCTGACATTAAGACACACCTCTCTGGATGCCCTGGAGGGGC
 CTCGAAAGCCCTTCATTAACAATTTATTATCACTAAAAAAA
 TGAATGTAGTGTGTCAGAGTACATGCCAGCTTCCTGTGGGCGGAGCTCAGCTGCACCTTAAGAAACCCAGGGCAGGAAACTGGCTGTTTGTATAGCAGAGAGAAAAAGTTGCAGT

FIG. 27I

1081 GGGCCCTTCGGGTGGCGCCAGGTAGGCGAGGTGGCCCGCGCGTGGAGGCAGGAGATGCGACTCTCCAAAACCCCTCGTCGACATG
 AspMetAlaAspTyrSerAlaAlaLeuAspProAlaTyrThrLeuGluPheGluAsnValGlnValLeuThrMetGlyAsnG(1y)³⁰
 1171 GACATGGCCGACTACAGTCTGCACTGGACCCAGCCTACACCCCTGGAAATTGAGAAATGTGCAGGTGTGACGATGGGCAATG GTAGG
 1261 TGGGGGCAGATGTGCCCAGGTGTGCCAGTGGGGGCGAGGTGTGCTGGGTCCAGGAGCAGATCTTTGGCACTCAACTTTGGGGTGGGAGGA
 1351 GAATGATACAAAATGGTAGGTTGGTCTCTACAGGCCAGCACAGGTGTGGCCAAAGTGAAGCCCATGTGCCAGGCACAGTGATCAGAGGCAT
 1441 TCTGGGTGAAGGAGGCTGCAAGGGCCAATTTCAGCAAAAGTCGATCCCGGCTATTCTCCAG GCCCTTCCAGTCCCTCACTGCCTCA
 Exon 1C (G)lyProSerSerProHisCysLeuT
 A

FIG. 28C

2071 CATAGAGCACATGCGTTTGTGCAATGCGGACCTGTGGAGTGCCTCTCTCTCGCATCTTATCCGTATGCGCGTTTGTCTGTGCGCC
 E1BF →
 2161 CATATTGTACCTGCTGTGTATATATGCAGTTCCCTGTGCTGCGGGCGGGGTCAACGGTCTCTGTGTGCACGACTGCACAGACCCAAA
 A
 2251 TGCAGGACTCTGTGTTGCCACTCACCAAGTGAGATTATATACCAACATGTCCGTTTGTCTCTGTGAGCAG ATTTGTGTCGCGCTGCGTC
 Exon 1B IleLeuLeuProLeuArgL
 euAlaArgLeuArgHisProLeuArgHisHisTrpSerIleSerGlyGlyValAspSerSerProGlnGlyA(sp)
 2341 TCGCCAGATTGAGGCATCCCTCCGACATCACTGGAGCATATCTGGAGGGGTGACAGTTCTCCACAGGAG GTAGGGGAAAAAGAGGAGG
 G

FIG. 28E

2431 CCCGAAACCCCTCCTGGAGGGAAGAGCCCCCATCGGTCCAGGCCAGCCTCAGAGAGAGGGGCGAGCAGCTGGCTGAGGTCAGCCTGC
 2521 CACCCCTGCTTCTTCTGTGTCTTGGAGCCACTCAGCCAGTATGAGGCTGCAGCTCCAGCTGAGGTCTGGAATCTTGTGGTCAGCTCAGCT
 2611 AGGGTGAGGAGGCGAGCTGCTGGGCACTGCTTGTGTCAGCTCAGCAGGTGCTCACCTGCCCTGCCCTCAGTCACGTGTGACCTTGGGC
 2701 ATGTCACCTCCCCATCCTGGCTTCTGTATCTTCTACAAACAGGCTTTCATCCCCCAGGCCCTGCTGGCTGGACGGCTTTAGGCCTGTC
 2791 TGAGGACCAACGCCAGGAGCGCAAGGCAAAACACACCAGAGAT::: 4.4 kb :::::CCCCTTGGGAGTTAGGAGGCCGGCTCC
 2881 CACCCAGAGGTGGCCAGGTTTTCATGCCCTTCTAGAGAAAGCTGGGCTGGTGGCTCCACCACAGGGAGACGCAGACCCCTCAGAAAC
 2971 AAGTCTGTGAAGTCACAAACCAGCCCCAGTTTACAGATGTGAACTGAAGCTCCAAAGTCAGGAGGTCACTCAGTGGGAGGTGATGGA

FIG. 28F

3061 GTGGGAACAGCCCCAGATCTGGCTGAGGCCGAAGCCCTGGAGAGATCCCCGAAGGCTCCCTTAGATGGCTGACATTCCTGCTCTTCCCTG
E2F →

3151 AAGCCTCACCTCCCTTCTCTCTCTGGCCAG ACACGTCCCCATCAGAAGGCACCAACCTCAACGCGCCCAACAGCCTGGGTGTACAGCGCCCT
Exon 2 30

3241 uCysAlaIleCysGlyAspArgAlaThrGlyLysHisTyrGlyAlaSerSerCysAspGlyCysLysGlyPhePheArgArgSerValArg
GTGTGCCATCTGCGGGGACCGGCCACGGSCAAACACTACGTGTCCTCGAGCTGACGGCTGCAAGGGCTTCTTCCGAGGAGACCGTGCG.

3331 gLysAsnHisMetTyrSerCysArg (g)
GAAGAACACATGTACTCCCTGCAG GTGAGGAGCCCTCAATTTCTCAGCTGGGHAATGGGCACACTGGGCTCATGSCCCCCAAGGTCTGTGTC
← E2R

3421 TTCTCCCTGAGTGGGTAAGGTCACAGACAGCTGCCCTTCAGGGCCCTCAAGGCTCTCTCTGGTTTGTAAAAAGACTTTGTGAATCCCAAGA

FIG. 28G

3511 AGAGCATCTATTCTAGGAACACACATTTACTGATCATCAAGCTACTGGCTGCCGTTTATTGAGCTCTTATCATATGCCAGGCACAACTACTA
3601 AGTCTTTTGTGTATTAC::: 1.6 kb :::::GTACTCCAGAGGTCAAGGTTCCCAACTCAGCTCTAACACCAACCAGCAGAG
3691 CGACCCAGGACCAACATGTTGCCTCTCTGAGCCCTCAGTTTCCCATGTTTAGCAGGACAGGACTGGGCTCTTAGAGAGTTTCATAGCACCTT
3781 TCCAGCTCCTGGTGGTTCAAGAGAGAACTCCCGGGATGAAGAGATGAGACACTGAGGTTGGGGGGTCAACTGGATAGCCAGGGCCCTA
3871 GTTCTCTCCTAAGAGAGGAAGTTGTGTCTTCTCCATCCCAACCATCCAAAGCCCTCCCCAG ATTTAGCCCGCAGTCCGTGTGGACAAAG,
E3F →
Exon 3⁸⁸ (Ar) gPheSerArgGlnCysValValAspLysA

FIG. 28H

sDlysArgAsnGlnCysArgTyrCysArgLeuLysLysCysPheArgAlaGlyMetLysLysGluA(1a)¹²⁰
 3961 ACAAGAGGAACCAAGTCCCGCTACTGCAGGCTCAAGAAATGCTTCGGGCTGGCATGAAGAAGAAG GTGAGCCTCGGCCCTCCCCGCCCC
 4051 ACCACCACTGCCCCACCTGCACCCACAGCTCCCCGACAGTCATTACAAGTGTAGCCACACTTTATGACTCAGTGGCAGGCCCCAGGGTG
 4141 ACTGGCTAATGGCTGAGAAGAGGGAGGGCTGGAAATCTGACCATAGGAGCGGCTGGCTTGGTCTTGAGAAAGATTC:::~::~:
 4231 5.9 kb ::TCCCACCTCCTCATCAGTCACAGACACCCCAACCCCTACTCCATCCCTGTCTCCCTCCTCACCTCTCTGTGCTCCTCCTCAC
 E4F → Exon 4

FIG. 28I

120
 (A) laValGlnAsnGluArgAspArgIleSerThrArgArgSerSerTyrGluAspSerSerLeuPheSerIleAsnAlaLeuLeuGlnAl
 4321 AG CCGTCCAGAATGAGCGGGACCGGATCAGCAGCTCGAAGGTCAAGCTATGAGGACAGCAGCCTGCCCTCCATCAATGGCTCCTGCAGGC
 155 T(R127W) : (T/I130)
 aGluValLeuSerArgGln
 4411 GGAGGTCTGTCCCGACAG GTACCGGGGTGATCTGCCACCCACCCAGGGATCCCCCACACTACAGAGGAGCTCACCTCCTCCACCTCCA
 4501 TTCTCCCCAGCCAGCCCTGGAGCAGCTGACGGGAGGGCCCTCAGATATTACAGAGGGACACTGAGTGGGTTTCACATGGGCCCAAGTTT
 E4R
 4591 GCAGCAAGGGCAGGAATCGAACCTGGCGCCCTGGGGCACTTTCTAATTCTATCTGCTGCTCCACAGGCCCAAGCAGAGTCTTCAC
 4681 CTTCACTGAGGGCCTGGGATCAGCTCAGTCCGAGAGAACAGAGCAGTGGCTCAGTGGAGAGAGGTGGCAAAAGTGGGGCCCAAGCCCTTCC

FIG. 28J

4771 CTTGCTGAGTGACCTTGGGCAAGTCACAGCACCTCTCTGAGCCATGGTTGCCCTCATGTCAGAAAAGGATGATGATTTTGTGCCCTGCCTT
 4861 CTCCTCTAAGGCTGACAGACTCCTTGGGGCTCTAAAGCTG::: 1.0 kb :::::TTCTCCCTCATCCCTGCCTCCTCCCTCCCT
 4951 CCGTTTTTACCCTGAGCTTCTTCAGAGCTGGAGGGCACCCACTATCCAGCCCCCTCCCCACATCTGATTCACGGAGGGGGCTCTGTGC
 5041 AGGGGACAGAGATGCGGGAGGGGGCGGACATCTCCAGCATTTTCTCCCTGTATCTCTCGAAG ATCACCTCCCCCGTCTCCGGGATCAA
 E5F → Exon 5 156 IleThrSerProValSerGlyIleAs
 nGlyAspIleArgAlaLysLysIleAlaSerIleAlaAspValCysGluSerMetLysGluGlnLeuLeuValGluTrpAlaLy
 5131 CCGCGACATTCGGGCGAAGAAGATTGCCAGCATCGCAGATGTGTGAGTCCATGAAGAGCAGCTGCTGTTCTCTCGTTGAGTGGGCCAA

FIG. 28K

sTyrIleProAlaPheCysGluLeuProLeuAspGln¹⁹⁷
 5221 GTACATCCCAGCTTCTGCGAGCTCCCCCTGGACGACCAG GTGAGGATGGCGTGATGGTGGCAGTAGTGGCAGTGGCGGGGCAGC
 5311 CAGGGGGCTGCTGGCCACCCTGGGATATAGCCCGTGGACTGGCTTGTATTTTATTTAACAATAATATGTAGTGCACACACGTGTCTGA
 5401 AACTTAAATCACCCTTACAAATATTAACCTCAGTTAGCTCTCTCCAAACAACCTCTATGAGGTAGGTACTAAGGTACTATTACTGCCATCT
 5491 CATAGGTGAGGAGATTGGGGGCACAGAGAGGTTAAGTAACCTGCTCAAGGTCACATAGCTACTATCCAGCATAGCTGGG::: 4.3 kb
 5581 :::::ATTTTACAAAGCACCCTTCATTAATTCCTCCATAGCTGGTCCATGGGTGGAAATTTGGGACCCACAGTTTGGAACTTTTGG
 5671 GATCATAGACCTTTTGGAGAACTCAAAAAGAAAAAGCACACAGAAATGTTGCTTACAGTTTCAATCAGGCGCACAGAGAGGCCCA
 5761 GCACGAAGCAGTTTCTTGCCCAAGGACACAGCAGTTCAAGGACAGAGTCAGCGGAGGTCTCTCAGCTCTGAGCATGTCTTTCCCT

FIG. 28L

5851 TCCAGGTTTCTAGTTTATGGGTAGTAGTTTATGATGCCCATTTTCACAGTTCAGGCAGGTAGAGGAGGGAGCATTAAAGCTGACTT
 5941 GCCAGCGTCACTGAGTTGGCTACGGGCAGCCTTCCCAAGGTACAGATGGCAACACTGTTCCTTCTCTTTTCAG GTGGCCCTGCTCA ValAlaLeuLeuA
 6031 rgAlaHisAlaGlyGluHisLeuLeuLeuGlyAlaThrLysArgSerMetValPheLysAspValLeuLeuGly(ly) Exon 6 198
 6121 GAGCCCATGCTGGCGAGCACCTGCTGCTCGGAGCCACCAAGAGATCCATGGTGTTCAGGACGTGCTCCTAG GTGAGGCGGCTGCCT
 6211 GCCCTGGCCAGGGCTCCAGGAGGGGTATGCCCTAGCATGGCCTCACCCAGGCAAGGAGATTACATGGTGGCATGCCAAGGGTGAGGGAGA
 6301 CTAGTCAGGAGTGGCCCTGTCTCAGGCTTGCAATGGAGGGCTCCAGGACTCAGTTTTCAACTGGGTACCCACTCAGATGCCAAGGAAAT
 GTGATGCAAGTCACCAAAATTCCACAGCATTCAGAGCAGCATCAGGGTTATCCCTGGAAATTACCTGTGCATCCTTTTCTTTTGA

FIG. 28M

6391 CAGAGTCTTGCTGTCACTCAGGCTGGAGTGCAATGATGTA: : : : : 1.4 kb : : : : : GCAAAACACTACCTATTTTAATATAACA
6481 ATGCTATGAGGGAGCTCGATTATTTATCCTCATCTTATAGATAAGAAAACTGAGGCACAGAGAGGTTAAAGTAACTTATCCAACTATAACC
6571 AGCTATCAGGGGCAGAGGCCATTAAAGCAGGCGAGTGCAGTCCAGAACTCTGGTCCCTTAACTTGAATGCTTTGGTGCCCTATCAGGTGACC
6661 TTTGAATGTCATCGATCTTGTGAGTCATGTTGGTAAATGGAGCTTGGGTCAATGTGAAAGAGGTCCTAGAAAGCCAAAGTTCCAAAGCTCAGC
6751 CGGATGACTCAAGGCAGCTTATCTTCTGAATCTGGGCCCTCAGCTTCCTTACCTGTGAAATGGGAGTCAACCATCCCTGCAGGTCTCCTCC
6841 CACAGGCACCAGCTATCTTSCCACTTAAAGCCAAACTAGAGGAGAGGGGTCAACCCAAAGGTGACTTCCCATTCCTCCTCCCTCCCAA
E7F →

FIG. 28N

237
 Exon 7 (G)lyAsnAspTyrIleValProArgHisCysProGluLeuAlaGluMetSerArgValSerIleArgIleLeuAspGluLeuV
 6931 CCCTTCCAG GCAATGACTACATTGTCCCTCGCACTGCCGGAGCTGGCGGAGATGAGCCGGGTGCCATACGCATCCTTGACGAGCTGG
 allLeuProPheGlnGluLeuGlnIleAspAspAsnGluTyrAlaTyrLeuLysAlaIleIlePhePheAspProA(sp)
 7021 TGCTGCCCTTCCAGGAGCTGCAGATCGATGACAAATGAGTATGCCCTACCTCAAGGCCATCATCTTCTTTGACCCAG GTACAGTGCACACCT
 T(Q268X)
 C
 7111 CCTAAGCCATCCCTGACTCTCTCTCCAGAACGGCTCTGCGAGACTTCTCTTATTGGGTTCGTACACTGAGTTCACAGCCCTCATCTCATGT
 E/R
 7201 TAACGACACGCCAGGAGAGGCCGTTTTCATTTAACAGATGAGGCAAGTCAAGATTGAAAGAGACAAATATGGCCGGGCGCAGTGGCTCACAC
 7291 CTGTAAATCCCATCACTTTGGGAGGCTGAGGCGGCGGATCACCTGAGGTCAAGGTCAAGATGAGCCTGGCTAACATGGAGAAACCCCAT

FIG. 280

7381 CTCTACTTAAAA::: 1.5 kb :::: GTGGCTCTGCCAACAACCTGGCTGTGGACCCAGGACAAGTCCCTATCTTTGCACTGTGT
7471 CTGGGTTTCCCGGTGTGAAGATGAGGCGGTTGCTAGGTGCTTATTGGATGCAATTCCTCAAGTCCCGCCCTCCATCTCCTATTCCCTCT
7561 CTTCTGGTTTAGTGTCTTTAGGAATGTGCAGAAATCTTTTCTGCCCTGTGTCTAGGAATCATAATTCATGCTGGCGTACCCCTGTTGT
7651 TGAGTCCCTGAATCCCTTGTGCCACACACTGCTGAAGACTCCTTTGTGTGACACACAAGTCAAGGGGACATCTGGGTCTTGACTCCCCCAGATGCT
Exon 8 289
7741 CCAGCTGGACCCCTGCTGCCCTCCCTTGCCACCCCTCTTCCATTGTAG ATGCCAAGGGGCTGAGCGATCCAGGGAAGATCAAGCGGCTGCG

FIG. 28P

7831 gSerGlnValGlnValSerLeuGluAspTyrIleAsnAspArgGlnTyrAspSerArgGlyArgPheGlyGluLeuLeuLeuLeuPr
 TTCCCAGGTGCAGGTGAGCTTGGAGACTACATCAACGACCGCCAGTATGACTCGGTGGCCGCTTTGGAGAGCTGCTGCTGCTGCC

7921 oThrLeuGluSerIleThrTrpGlnMetIleGluGlnIleGlnPheIleLeuPheGlyMetAlaLysIleAspAsnLeuLeuGlnG1
 CACCTTGCAGAGCATCACCTGGCAGATGATCGAGCAGATCCAGTTTCATCAAGCTCTTCGGCATGGCCAAGATTGACACACCTGTTGCAGGA

8011 uMetLeuLeuGlyG(ly)³⁶⁸
 GATGCTGCTGGGAG G P C Q A Q E G R G W S G D S P G D R P H T V S S P

8101 CCTCAGCTCCTTGGCTTCCCCACTGTGTGCCGCTTGGCAAGTTGCTTAACCTGTCTGTGCCCTCAGTTTCTCTCACCAGAAAAATGGGAACA
 L S S L A S P L C R F G Q V A

FIG. 28Q

8641 CCTTCAACTCACTTTGTCTCTTGGTTTTTGGGGTCCCTCTTAACACCCCTCATGAAGTCTATAGATGGGAATGGTACACCCTAGTTTA
8731 CTAACCCAGGAATAGGTACCCAACAGGCACTGCCAATATTTGGATGGGCTGGTTGATTTGGCCACGCCCTGAGGAAGATGGCGTCCCAAGGCC
8821 TGAGGTCTGCATCCAGACTCTCCATCCTGATCGACCTTCTCTACCTGCAG GGTCCCCCAGCGATGCACCCCATGCCACACCCCTGC
Exon 9 368
(G) lyserProSerAspAlaProHisAlaHisProLeuH
isProHisLeuMetGlnGluHisMetGlyThrAsnValIleValAlaAsnThrMetProThrHisLeuSerAsnGlyGlnMetCysGluT
8911 ACCCTCACCTGATGCAGGAACATATGGGAACCAACGTCATCGTTGCCAACACAATGCCCACTCACCTCAGCAACGGACAGATGTGTGAGT
419
pProArgProArgGlyGlnAlaA(1a)
9001 GGCCCCGACCCAGGGACAGGCAG GTGGGCAAACTCTGGGATTTTACCTTGCAAAGGTGAGGATGGGGCTTAAGACAGGAGGCAGGAGA

FIG. 28S

9091 AAGTGGAGTCTAGAAAGGTAGAACACAGGATGCCAACAGTTTCTGGGTTCCAGGGTAGGGNATAAAGGGCAAGATGTCCATTGTGTGAGGC
 9181 TGTATTATTCAGTAAGGTGACTGACAGCCCTTTACTGAATGAAGCCATTGTGGGATGAGGCAATCCCACTGGATGAGGTAACCCATTGGGTG
 9271 AAGATGCTCTTGGGTGAGAAATCCCATTTAGTTGACATTGTCCATTAAAGTAAAGTGGTCATTGAAGTAAGGCTGCACAGTTGGGTAAGGCTA
 9361 TCCATTAGACATTAGATGAGACTACCCATTGGGTCAGGATGTCTGCTGGGCTA::: 1.4 kb ::::TTTGGGAGAACAGTCC
 9451 AAGTCTGCATATCAAAATAAATGATGGAGAGATGGGTGGTAGGACCTTCCAGACCTCATAAACTTAGGCTTTATGATCTGGGACTCACA

FIG. 28T

9541 GAAGTTGAGCAATAAAGACCTTAGGATATCTGGCTTAATTAATCTCTCATTTTATAGAGGAAGAATTAAAGTCAAGGTGGGGCAG

9631 GGTGGAGGGGAGAACTTTCCCGGGGCTCTTCATTACTCCACAAAGGCTGGAATTTTGAGCAGCCCCCTGCTGTCTGTTTGTCTTCC
 419
 (A) laThrProGluThrProGlnProSerProProGlyGlySerGlySerGluProTyrlLysLeuLeuProGlyAlaValAlaThrIleVa
 9721 AG CCACCCCTGAGACCCCAAGCCCTCACCGCCAGGTGGCTCAGGCTGTGAGCCCTATAAGCTCTGCCGGGAGCCGTCGCCACAATCGT
 465
 9811 lLysProLeuSerAlaIleProGlnProThrIleThrLysGlnGluValIleOP
 CAAAGCCCTCTCTGCCATCCCCCAGCGACCATCACCAAGCAGGAAGTTATCTAGCAAGCCGCTGGGGCTTGGGGCTCCACTGGCTCCC

FIG. 28U

9901 CCCAGCCCCCTAAGAGAGCACCCTGGTGATCAGTGTACGGCAAGGAAGACGTGATGCCAGGACCAGTCCCAGAGCAGGAATGGGAAG
 9991 GATGAAGGGCCCCGAGAACATGGCCCTAAGGCACATCCCACTGCACCCCTGACGCCCTGCTCTGATAACAAGACTTTGACTTTGGGGAGACCCCT
 10081 CTACTGCCCTTGGACAACTTCTCATGTTGAAGCCACTGCCCTTCACTTCACTTCATCCATGTCCAAACCCCGACTTCATCCCAAAGGAC
 10171 AGCCGCCCTGGAGATGACTTGAGCCTTAC

FIG. 28V